ASSESSMENT OF HEALTH RELATED QUALITY OF LIFE IN CHILDREN WITH EPILEPSY USING QUALITY OF LIFE IN CHILDHOOD EPILEPSY QUESTIONNAIRE (QOLCE-55)

A Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,

CHENNAI- 600 032

In partial fulfilment of the award of the degree of

MASTER OF PHARMACY

IN

Branch-VII –PHARMACY PRACTICE

Submitted by

Name: NAGARAJAN .S

REG.No.261640207

Under the Guidance of

Dr. N. VENKATESWARAMURTHY, M.Pharm., PhD,

DEPARTMENT OF PHARMACY PRACTICE

J.K.K. NATTRAJA COLLEGE OF PHARMACY

KUMARAPALAYAM – 638183

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CERTIFICATES

EVALUATION CERTIFICATE

This is to certify that the dissertation work entitled **"Assessment of Health Related Quality of Life in Children with Epilepsy using Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55)"** submitted by the student bearing **[REG.No.261640207]** to **"The Tamil Nadu Dr. M.G.R. Medical University"**, Chennai, in partial fulfillment for the award of Degree of **Master of Pharmacy** in **Pharmacy Practice** was evaluated by us during the examination held on.....

Internal Examiner **External Examiner**

CERTIFICATE

This is to certify that the dissertation **"Assessment of Health Related Quality of Life in Children with Epilepsy using Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55)"**is a bonafide work done by **Reg.No.261640207,** Department of Pharmacy Practice, J.K.K. Nattraja College of Pharmacy, Kumarapalayam, in partial fulfillment of the University rules and regulations for award of **Master of Pharmacy** in **Pharmacy Practice** under my guidance and supervision during the academic year 2016-2017.

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DECLARATION

DECLARATION

I do hereby declared that the dissertation **"Assessment of Health Related Quality of Life in Children with Epilepsy using Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55)",** submitted to "**The Tamil Nadu Dr. M.G.R Medical University"**, Chennai, for the partial fulfillment of the degree of **Master of Pharmacy** in **Pharmacy Practice,** It is a bonafide research work has been carried out by me during the academic year 2016-2017, under the guidance and supervision of **Dr. N. Venkateswaramurthy, M.Pharm., Ph.D.,** Professor, Head, Department of Pharmacy practice, J.K.K. Nattraja College of Pharmacy, Kumarapalayam.

I further declare that this work is original and this dissertation has not been submitted previously for the award of any other degree, diploma, associate ship and fellowship or any other similar title. The information furnished in this dissertation is genuine to the best of my knowledge.

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INTRODUCTION

1. INTRODUCTION

Epilepsy is suspected when there is repetition of seizures. The cause and clinical spectrum of epilepsy are extremely wide-ranging in children. Although for practical purposes, epilepsy might still be a useful diagnostic category, it would be inappropriate to regard it as a single entity. This Seminar aims to critically review the main concepts that underlie classification of seizures and epilepsies in children, the rationale for prognostic considerations and for choosing complimentary investigations, and treatment.[1]

Definitions and terminology

Seizures are described with standard terminology,[2-5] and, where possible, classified in specific epilepsy types or syndromes[4,6] (panel 1 and table 1). A syndrome is a complex of signs and symptoms defining a unique epilepsy condition.[4] Syndromes are classified on the basis of seizure types, clinical context, neurophysiology, and neuroroimaging.[4,6] Epilepsy can be generalised, if all seizures and electroencephalogram (EEG) abnormalities are generalised, or focal (partial) if clinical and EEG manifestations suggest focal onset, but this distinction is not always clear cut.[4] Idiopathic epilepsies are not associated with any brain lesions; they are caused by a complex genetic predisposition or, rarely, single-gene inheritance. Symptomatic epilepsies result from a brain lesion, which is not necessarily detected by neuroimaging.

The term cryptogenic is synonymous with presumed symptomatic.[4] Syndrome diagnosis is helpful in guiding investigations, and management, and is an early prognostic indicator.

Epidemiology

Worldwide, it is estimated that 10·5 million children under 15 years have active epilepsy, representing about 25% of the global epilepsy population. Of the 3·5 million people who develop epilepsy annually, 40% are younger than 15 years, and more than 80% live in developing countries.[7] Population-based studies on childhood-onset epilepsy6 indicate annual incidence rates of 61–124 per 100 000 in developing countries, and 41–50 per 100000 in developed countries.[7] Incidence falls progressively from around 150 per 100 000 in the first year of life to 45–50 per 100000 after the age of 9 years.6 Cumulative incidence studies indicate that up to the age of 15 years, 1·0–1·7% of children will have at least one unprovoked seizure, and 0·7–0·8% repeated seizures.[8,9] Frequency rates in Europe and North America vary from 3·6–6·5 per 1000, whereas African and Latin American studies report rates of 6·6–17 per 1000.[7]

Natural history

In children who experience a first unprovoked focal or generalised tonic-clonic seizure, the cumulative risk of recurrence is 42% at 8 years' follow-up, with only 3% of all recurrencies occurring after 5 years. Multivariable analysis has shown that risk factors for recurrence include a remote symptomatic cause, an abnormal EEG, a seizure occurring when asleep, a history of febrile seizures, and postictal paresis.[10] Treatment does not change the recurrence rates.[11,12] About 64% of individuals that have had seizures in childhood will be in remission (_5 years) in adulthood.[13] Of these patients, only 16% will be still on medication. The practical implications of these figures are limited, however, if specific epilepsy syndromes and causes are not considered.

About 75% of patients of all ages reach remission on antiepileptic drugs, but attempts at drug withdrawal after 3 years of seizure control are followed by a relapse in 25% of patients.[14] However, relapsing rates are highly variable in different epilepsy syndromes: 0% for benign rolandic epilepsy, 12% for childhood absence epilepsy, 29% for focal symptomatic epilepsies, and 80% for juvenile myoclonic epilepsy.[15]

General aspects of prognosis

Most children with epilepsy can be divided into four main prognostic groups.[16] The first group is the benign epilepsies—eg, benign rolandic epilepsy (20–30% of patients), in which remission occurs after a few years and treatment can often be avoided. The second group is the pharmacosensitive epilepsies—eg, most children with absence epilepsy (30% of patients), in which seizure control is easily achieved by medication and spontaneous remission occurs after a few years. The third one is the pharmacodependent epilepsies, in which drug treatment will control seizures, but no spontaneous remission occurs—eg, juvenile myoclonic epilepsy and many cases of symptomatic focal epilepsy (20% of patients). Drug withdrawal is followed by relapse and treatment will be lifelong. The fourth group is the pharmacoresistant (or refractory) epilepsies, with poor prognosis (13–17% of patients). The definition of pharmacoresistance is arbitrary and refers to both the frequency and severity of seizures for an individual child. Resistance to drugs can usually be predicted early after an inadequate response to initial appropriate treatment.[17] Although benign epilepsies and most pharmacosensitive idiopathic generalised epilepsies can be identified early after onset, for many children with focal symptomatic or presumed symptomatic epilepsies, and for some of those with idiopathic generalised epilepsies, pharmacosensitivity or pharmacodependence are often defined accurately only in

retrospect. Early response to drugs (75–100% seizure reduction within the first 3 months of treatment) is a good predictor of long-term remission, irrespective of the cause. However, idiopathic and presumed symptomatic epilepsies are three times as likely to achieve remission than symptomatic forms.[13]

Co-morbidities in infantile epilepsies learning and development

Because of the often severe nature of underlying symptomatic etiologies and often frequent seizures in infantile epilepsies, early developmental attainments and learning may be impaired or previously acquired skills lost. This may also apply to those infants in whom no cause for the epilepsy has been identified. This is well illustrated by infants with drug resistant cryptogenic/presumed symptomatic West syndrome. An infant with apparently normal early development begins to lose previously attained skills around the onset of spasms. Conversely, a rapid and sustained clinical and EEG response to treatment in WS can lead to a recovery of lost skills, particularly visual behavior and social interaction. Nevertheless, despite this recovery, most infants with even cryptogenic WS are left with significant intellectual disability. The precise relationship between the seizures, EEG changes and developmental impairment is as yet unknown and remains an active area of research. A study of infants with WS caused by trisomy 21 showed that those diagnosed (and therefore treated) after eight weeks showed a poorer response in terms of spasm suppression and had a poorer developmental outcome and showed more autistic features; this was not entirely related to persistence of spasms in the group of children diagnosed after eight weeks.[19] This suggests that both early and effective treatment for West syndrome is critical. Clearly, these data need to be confirmed in other groups of infants with WS caused by specific etiologies.

Family adjustment

Epilepsy that occurs at any age can be very distressing and may cause significant and often intolerable stress on the family, including older siblings. This is particularly significant in those families where the child is an infant (with their 'whole life ahead of them') and the seizures are frequent and often prolonged, resulting in frequent hospitalizations. These children also experience school difficulties not only because of the effect of frequent seizures and persistently 'epileptic' activity on the EEG, but also through disrupted school attendance. It is obviously very important that parents be given honest and realistic advice about their child's epilepsy as well as the support and access to medical services that they will frequently require. Epilepsy nurse specialists are extremely valuable in these situations, establishing a clear link between the hospital-based services and the child's home and school.

What to do if the first drug fails?

The failure of a first antiepileptic drug (AED) to control seizures should lead to a careful reappraisal of the child's problem including: have they been receiving the antiepileptic medication on a regular and consistent basis? does the child really have epilepsy? if 'yes,' has the correct seizure type and epilepsy syndrome been diagnosed? has an underlying cause been considered and actively sought? It is always important to ask about the development of any new paroxysmal events or seizure types: myoclonic and some focal seizures can be subtle, easily overlooked or dismissed by parents/carers. Sometimes the correct syndrome will only become apparent over time, and this may be months rather than weeks.

For example, children with Dravet syndrome present with febrile tonic-clonic seizures in the first year of life and the myoclonic and absence seizure only subsequently present in the second or third year of life.

A review of the seizure type and syndrome may also include repeating investigations and specifically the EEG. Prolonged video–EEG recordings are useful if any doubts remain about the nature of paroxysmal events. The possibility that the patient may have one of the early-onset neuro-degenerative disorders should also be considered, even if there were no clues to this diagnosis at the onset. Failure to achieve developmental milestones or even loss of previously acquired milestones, changing or new neurological symptoms and signs, abnormal head growth (acquired micro- or macrocephaly) or even subtle behavioral changes can all be important clues to a possible underlying neuro-degenerative disorder. Prominent myoclonic seizures in particular are often associated with the neuro-degenerative disorders and specifically a metabolic disorder. The most commonly encountered metabolic disorders at this age will be late infantile neuronal ceroid lipofuscinosis ('Batten's disease') and progressive neuronal degeneration of childhood with or without liver disease (Alpers' disease).

Other than poor seizure control as determined by the natural history of the epilepsy syndrome, the next most common reason for failure of a first medication is an unacceptable side effect. Many side effects in infancy are predictable and can be reduced or avoided by slow-dose titration. However, rapid changes in hepatic and renal elimination of drugs can give rise to rapid changes in plasma concentration as the infant grows; this is particularly illustrated by phenytoin, a difficult drug to titrate at the best of

times, although fortunately this drug is only rarely used in the treatment of the infantile epilepsies.

Once the decision to change medication has been made the first decision is whether to directly substitute medication and maintain monotherapy, or whether to use combination therapy. In general, sequential monotherapy should be the principle, and combination therapy reserved until there have been at least two attempts at monotherapy. If treatment with multiple antiepileptic drugs is required (as occasionally in WS and very commonly in Dravet syndrome and migrating partial seizures in infancy), the number should be kept to a minimum, and ideally no more than two used simultaneously. Three drugs should be used only very rarely; first, because there are no convincing data that three are more effective than two,and second because of the risk of adverse side effects, including on the infant's development and behavior.

Syndrome-specific therapy

Middle treatment of WS will depend on the response to initial treatment. If complete seizure control is achieved with resolution of the hypsarrhythmic EEG pattern, vigabatrin is usually continued for approximately four, or at most, six months before being withdrawn. When spasms stop with hormone treatment, usually the hormone treatment is gradually withdrawn over one to three months; there is a higher risk and rate of relapse if withdrawal is over one month. If spasms return, then a second course of hormone treatment is often undertaken and if that fails then vigabatrin or other more conventional medications such as sodium valproate or nitrazepam will be prescribed, possibly determined by the underlying etiology.

Alternative treatments for epilepsy in infancy

Epilepsy surgery

Epilepsy surgery, with techniques initially developed in adult practice and subsequently modified for the pediatric population, is the only current therapy that can result in a 'cure' for refractory epilepsy. It is important to both appreciate and emphasize that surgery can, and should, be performed whenever this is appropriate. This includes in infants and young children because years of frequent and drug resistant epilepsy may result in irreversible cognitive (educational) and behavioral consequences which could potentially be prevented by early and curative surgery.

There are two main types of operation:

Resective surgery the objective is to remove the epileptogenic zone or lesion responsible for the seizures.[20] Palliative surgery the objective is to reduce the frequency or severity of seizures, sometimes by targeting specific seizure types, and specifically 'drop attacks' (tonic or atonic seizures). The two main types of palliative procedure are corpus callosotomy[21] and vagal nerve stimulator implantation.[22] Consideration of epilepsy surgery is reserved for patients with medically refractory epilepsy. There is no unanimous definition of 'medically refractory epilepsy' but pragmatically it is generally defined as a failure to achieve 12 months' seizure freedom with a minimum of two or possibly three appropriately prescribed antiepileptic medications. There are however a number of situations where epilepsy surgery should be considered early in the course of the disease.

These include: Infants with primary brain tumors who present with epileptic seizures Sturge Weber syndrome. This is a good example of a disorder in which the natural history

of the disease (refractory epilepsy, progressive hemiplegia, progressive cognitive impairment) can be altered by early resective surgery – in this case hemispherectomy or hemispherotomy (the latter term refers to disconnection rather than removal of the abnormal hemisphere).

A perhaps more common epilepsy syndrome which may be amenable to surgery is West syndrome and where there is an obvious focal lesion including focal cortical dysplasia, a porencephalic cyst (secondary to a congenital or peri-natally acquired stroke) or an epileptogenic tuber in tuberous sclerosis. Reported seizure freedom rates in selected groups of patients are as high as 65% and most of these patients have already failed with many antiepileptic drug treatments. It is tempting to consider that early targeted surgical treatment may improve neuro-developmental and cognitive outcome in a proportion of children with an infantile epilepsy.

The role of vagal nerve stimulation (VNS) in the treatment of all the epilepsies, and particularly the epilepsy syndromes of infancy, remains uncertain. Although technically more difficult in infants, VNS can and has been undertaken in migrating partial seizures of infancy, Dravet syndrome and West syndrome.[22]

Ketogenic diet

The ketogenic diet, with appropriate instigation, close dietetic monitoring and follow-up, is a viable option for infants with medically refractory epilepsy who are unable to undergo epilepsy surgery.[23] There are currently three variants:

- Classical (largely food-based).

- Medium chain triglyceride (MCT; largely liquid-based). This is the preferred variant for infants with feeding gastrostomy tubes in situ.

- Modified Atkins (the most 'relaxed' and least restricting of the three variants).

The traditional ('classical') ketogenic diet is carefully calculated to provide a certain ratio (grams of fat : grams of protein and carbohydrate) which usually ranges 3–4 : 1. The other two variants (median chain triglyceride [MCT] and modified Atkins) are generally more palatable and therefore better tolerated – particularly in older children.[24,25] The MCT variant is usually the more appropriate one to use in infants and young children, who are fed through a feeding gastrostomy tube.

There are two rare disorders, pyruvate dehydrogenase complex deficiency and glucose transporter (GLUT-1) deficiency syndrome, for which the treatment of choice is the ketogenic diet. The seizures and movement disorders in these conditions often show a dramatic response. The ketogenic diet is being increasingly used earlier in the course of the epilepsy when initial medications fail in many infants with other metabolic disorders or epilepsy syndromes. Evidence suggests that the infant brain is better than the adult brain in utilizing ketone bodies as an alternative energy substrate. It is also clear that the diet is better tolerated in infants and young children than in teenagers and adults.

The diet must be adhered to tightly and this can be difficult or impossible for the infants and their families. Assuming it is closely adhered to, a period of at least four to eight weeks will be adequate to determine if it has been effective and whether it should be continued (a good response) or withdrawn (no response or a poor response). In terms of efficacy, most of the published data on the use of the ketogenic diet in infancy is in the more severe epilepsy syndromes and particularly West and Dravet syndromes. Overall, it

seems that approximately one-third of these infants will have a good response to the diet. One non-randomized, retrospective study compared ACTH and the diet as the initial treatment of infantile spasms and found no statistical difference in efficacy or time to spasm freedom,[30] although ACTH was close to showing a superior effect (p¼0.06). Predictably, there was a lower incidence of side effects in infants treated with the diet. However, it must be recognized that the diet is both an abnormal and complex diet and infants will require vitamin and mineral supplements and close clinical, biochemical and hematological monitoring. Nevertheless, the diet does merit consideration early in the course of the infantile epilepsies, particularly in the more severe epilepsy syndromes, including migrating partial seizures in infancy. It can only be initiated, and closely monitored by a tertiary epilepsy centre.

Later treatment of infantile epilepsies

Prognosis of epilepsy presenting in infancy

As might be expected, the prognosis of the more severe epilepsy syndromes of early infancy is generally poor in terms of the seizure outcome and, perhaps more importantly, the cognitive (particularly communication) and behavioral outcome. The outcome of the benign syndromes is generally good although the risk of later specific cognitive problems is probably still slightly greater than that of the general population.

West syndrome

Despite improvements in recognition of WS and the availability of newer treatments, published data from various sources (particularly Finland) suggest that the long-term outcome of infants with WS has not changed markedly over the past thirty years.[24] The

prognosis depends primarily on the underlying etiology. There is a small group of patients with normal early development prior to the onset of spasms, classical hypsarrhythmia, normal investigations including normal neuro-imaging and an excellent and sustained response to initial treatment that will have a normal or near normal cognitive outcome. This group, which constitutes between 5 and 10% of all infants with WS, is sometimes referred to as idiopathic WS, often because there is a strong family history of epilepsy, but not usually WS. Obviously, it may not be that easy to identify this group at initial presentation. In general however, the prognosis of West syndrome is usually very poor. In a large series from Finland, 65% of all patients had severe learning disability (intelligence quotient or developmental quotient less than 50), 76% still had epilepsy at the age of three and over 10% had a symptomatic generalized epilepsy.[27] These figures are very similar to reports in the 1960s and 70s. The main factor which predicted a poor outcome was having a symptomatic etiology.[28] Finally, there remains a slightly increased mortality rate which also has not changed significantly over the years; by 3 years of age 13% of the patients had died compared with 11% in the historical control group.

Dravet syndrome

Unfortunately, the long-term prognosis of Dravet syndrome is very poor. Children are usually developmentally normal prior to the onset of seizures. This is always followed by a regression in development which then plateaus at around five or six years of age. Overall intelligence in older school children is typically severely affected.[29] Conflicting evidence suggests that either language and communication, or visuo-spatial skills are predominantly affected. Behavioral difficulties are also frequent as manifest by hyperactivity, impulsivity and autistic traits. Seizures usually persist although they may

become less problematic as the patient gets older with the atypical absences and myoclonic seizures becoming less frequent and the tonic-clonic seizures being of shorter duration. Motor impairment, specifically acquired ataxia, is also seen in older children with Dravet syndrome and may be related to the dysfunction of sodium channels in the cerebellum or the seizures themselves, or a combination of factors.

Long-term studies of children with Dravet syndrome have suggested that the frequency of convulsive seizures (more than five a month) is associated with a worse cognitive outcome. It is therefore tempting to speculate that better initial control of seizures may improve cognitive outcome in these children. It remains to be seen if the use of more aggressive therapies including stiripentol or the ketogenic diet could alter the natural history of this devastating epilepsy syndrome. Finally, there is an increased mortality in Dravet syndrome as a result of convulsive status epilepticus, accidents including drowning and, possibly more importantly, sudden unexpected death in epilepsy (SUDEP). Approximately one in seven children with Dravet syndrome die before adolescence.

Migrating partial seizures in infancy

Although this is a relatively recently reported syndrome (and more long-term data are clearly required), the vast majority of infants show a very poor or poor outcome. This encompasses both seizure frequency and developmental functioning. In addition, a number of infants have died under five years of age, occasionally earlier.

Outcome of the benign epilepsy syndromes of infancy

The outcome of benign infantile convulsions, both familial and non-familial, is excellent with normal development and cognitive function. Seizures do not recur, even in the

patients who require treatment during infancy. There is no generally agreed consensus on how long these patients require treatment; it seems reasonable to treat for approximately six to twelve months and then withdraw medication. Benign myoclonic epilepsy of infancy is also reported to have a good outcome in terms of seizure control with the majority responding well to sodium valproate and spontaneous remission of seizures over a period of time. However, the cognitive outcome may not be as good. A recent literature review indicated that approximately one-third of patients had some degree of learning disability ranging from mild specific learning disability to more severe global cognitive impairments.[30]

COMORBIDITY [31]:

Neurological comorbidities Many factors may contribute to the development of neurological morbidities in children with epilepsy,[32] such as the detrimental effects of chronic seizures on brain development, the medications used to treat seizures, and possibly an independent effect of the physiological disturbances that predispose the brain to seizures. Neurological comorbidities in children with epilepsy are variable, including cognitive impairment, language impairment, migraine, and sleep problems. We will discuss these issues in the following sections.

Cognitive impairment

The association between mental retardation and epilepsy has been well described in the literature.[33] Children with epilepsy had high rates of grade retention and placement in special education compared with sibling controls.[34] Several population-based prevalence studies of children with epilepsy reported that intellectual disability (full-scale intelligence quotient < 70) was the most common comorbidity (30e40%).[35] However, the

long-term risk of learning problems exists even in those with normal IQs and wellcontrolled seizures.[34] Moreover, in a follow-up study the cognitive deficits associated with childhood-onset epilepsy, despite the duration of epilepsy, may remain consistent to 60 years of age.[36] The various epilepsy syndromes of childhood differ greatly in terms of cognitive outcome. Children with infantile spasms and Dravet syndrome (severe myoclonic epilepsy in infancy) usually have long-term cognitive and behavioral problems.[37] LennoxeGastaut syndrome is also associated with a poor prognosis in children.[38] Although "benign epilepsy" is supposed to have better prognosis in children, absence epilepsy has been reported to have an increased risk for neurocognitive impairment.[39] Some studies in the past also showed that children with symptomatic generalized epilepsy had a lower full-scale intelligence quotient than those with idiopathic generalized epilepsy and focal epilepsy,[40] and temporal lobe epilepsy specifically had much worse memory function than frontal lobe epilepsy and childhood absence epilepsy.[41] Many factors of childhood epilepsy may contribute to the development of cognitive impairment in children. Children with epilepsy and abnormal electroencephalograms scored lower than those with normal electroencephalograms on reading and spelling measures, even with comparable IQs.[34] Young age at onset, symptomatic cause, epileptic encephalopathy, and continued treatment of AEDs were also reported to be independently associated with cognitive outcome.[42,43] Older AEDs (prior to1990), such as phenobarbital, can produce greater cognitive impairment. However, carbamazepine, phenytoin, and valproic acid (VPA) are comparable in their cognitive effect.[44] Among the new AEDs, topiramate is reported to be significantly associated with memory and cognitive problems,[45] and the frequency of side effects in cognition is dose-related.[46] Oxcarbazepine, [47]lamotrigine,[48] and levetiracetam[49] are found to have no or few

adverse effects on cognition. Careful selection of AEDs, avoiding polytherapy, slow titration, and using the lowest effective AED dose are reported to decrease the cognitive side effects of AEDs in children with epilepsy.[44]

Language impairment

The language impairment in children with epilepsy may arise from a number of factors, including underlying neuropathology, the impact of seizures on the developing brain, the development of cognition, and the severity of epilepsy in children.[50] The occurrence of speech disorders may be as high as 27.5% in children with epilepsy.[33]

Compared with their siblings, children with epilepsy may also have significantly lower language scores in word knowledge, category fluency, and response to commands of increasing length and complexity,[51] especially in those with an earlier age of onset. Some epileptic syndromes have been well documented in association with language impairment. The LandaueKleffner syndrome (LKS) and the epilepsy with continuous spike waves during slow-wave sleep (CSWS) share several common features: both are age-related, first appear in childhood, and are characterized by mild epilepsy associated with severe neuropsychological dysfunction. Language disorders in LKS mainly involve comprehension with preservation of nonverbal intellectual functions.[52] Children with LKS have a variable prognosis. Some regain speech and others have permanent speech impairment.[37] By contrast, language disorders associated with CSWS are predominant in the areas of lexical and grammatical judgment, whereas comprehension is spared. Patients in remission and those in an active phase of CSWS have the same language impairment profiles.[53] Children with benign epilepsy with centrotemporal spikes, which is now recognized as lying on a spectrum with the LKS, may also have the comorbidity of mild

language impairment, mainly with oromotor performance and auditory discrimination, including poor tongue movements and articulation, and worse performance on dichotic listening.[54]

Migraine

The links between epilepsy and migraine have long been known but have been incompletely understood. Both are believed to result from brain hyperexcitability, and the therapeutic agents effective for each disorder may overlap.[55] Migraine and epilepsy are highly comorbid and individuals with each disorder are more than twice as likely to have the other.[56] Stevenson[57] reported a higher prevalence of migraine in children with epilepsy (14.7%) than in the general population (2.7e11%). Children with epilepsy had a 4.5-fold increased risk of developing migraine headache than tension-type headache.[58] The headaches usually start in the same year or after the diagnosis of epilepsy and occur mostly in children older than 10 years with idiopathic epilepsy.[59] Specifically, a strong association of epilepsy with rolandic paroxysms and migraine in children has been reported.[60] A controlled study revealed that migraine was more prevalent in children with benign epilepsy with centrotemporal spikes and juvenile myoclonic epilepsy.[61]

Sleep problems

It has been reported that children with epilepsy have significantly more sleep problems,[62] including parasomnias, parent/child interaction during the night, sleep fragmentation, daytime drowsiness, and bedtime difficulties.[63] Children with seizures also have more sleep problems than seizure-free children.[63] Evidence suggests that both the occurrence of seizures and AEDs are associated with significant sleep disruption. Persistent daytime drowsiness in children with epilepsy is not always due to the side effects of AEDs and

may arise from sleep fragmentation.[64] Children with epilepsy have longer stage 1 sleep percentage and latency to rapid eye movement (REM) sleep compared with controls.[65,66] It is also found that REM latency, length of apnea, and periodic leg movement in children with epilepsy correlated with depression, inattentiveness and hyperactivity, and/or oppositional behavior.[65] It is reported that continuous positive airway pressure treatment of obstructive sleep apnea, which is a specific type of sleep disorder, and more comorbid in children (20%) than in adults (10%) with epilepsy, improves seizure control, cognitive performance, and quality of life.[66] Moreover, a particular pattern of association has been found between nocturnal frontal lobe epilepsy and non-REM arousal parasomnias, the latter being found in the personal or family history of up to one-third of children with nocturnal frontal lobe epilepsy.[66]

Psychiatric comorbidities

Psychiatric comorbidities are common in children with epilepsy, and constitute a significant burden to the children and their families. Some studies have shown that a psychiatric disorder can emerge in children early in the course of their illness[67] or even prior to the onset of seizures.[68] The most common psychiatric disorders among children who have epilepsy include attention deficit/hyperactivity disorder (ADHD), and depressive and anxiety disorders. Although infrequent, psychosis, oppositional defiant, and tic disorders may occur in children who have epilepsy.[69,70]

Autism spectrum disorders

It is well documented that children with autism spectrum disorder (ASD) have an increased prevalence of seizures, which is estimated to be w20e25% of the whole spectrum.[71] However, the prevalence of ASD in children with epilepsy is rarely reported,

and varies depending on age, types of epilepsy, and method of evaluation. In a questionnaire-based study, as high as 32% of children fit the criteria of autism screening questionnaires for having ASD.[72] Most of them had not been previously diagnosed.

The children identified as being at risk of having ASD have right temporal lobe lesions,[73] worse behavior, daytime sleepiness, and a younger mean age of seizure onset, at ~2 years of age.[72] The high correlation between ASD, neurologic dysfunction, and epilepsy suggests an underlying encephalopathy presenting with a combination of neurologic abnormalities, including clinical epileptiform activity.[74]

ADHD

The prevalence of ADHD is estimated to be between 12% and 39% in children with epilepsy, and is much higher than 3e7% in the general population of children.[75] ADHD is significantly more prevalent in children with new-onset epilepsy compared to healthy controls (31% vs. 6%, respectively), and the predominant ADHD type is the inattentive type.[76] A population-based study using data from the Taiwan National Health Insurance Research Database revealed a 2.54-fold increased risk of subsequent ADHD in children with epilepsy compared to normal controls, and the age-specific risks increased with age, at 2.26-, 3.53-, and 5.30-fold for patients aged 0e6 years, 6e12 years, and 12e18 years, respectively.[77]

Symptoms of ADHD are more common in some specific types of epilepsies, such as frontal lobe epilepsy, childhood absence epilepsy, and rolandic epilepsy, and may antedate seizure onset in a significant proportion of cases.[78,79] In a study of Taiwanese children with epilepsy, a history of developmental delay predicted ADHD-related

symptoms and an earlier onset of epilepsy predicted inattention and hyperactivity/impulsivity.[80]

Mood disorders

Mood disorders had been reported in 12e26% of children with epilepsy.[81]Emotional disorders can be found in 16.7% of children with complicated epilepsy and in 16% of those with uncomplicated epilepsy compared with 4.2% in the general population.[82] Ott et al[83] reported mood disorders in 12% and 13% of children with complex partial seizures and childhood absence epilepsy, respectively.

In general, children with epilepsy display more internalizing problems (withdrawal, somatic complaints, anxiety, and depression symptoms) than they do externalizing problems such as acting out and conduct problems.[83] The higher ratings on the somatization and emotional withdrawal were found among children with poor seizure control.[84]

In addition to ADHD, the most common psychiatric disorders among children with epilepsy are depressive and anxiety disorders.[69] Seizure frequency,[85] AED polytherapy,[86,87] types of AEDs,[88,89] and duration of illness[86,87] are all related to the development of these comorbidities. The depression, which is more comorbid in those treated with phenobarbital,[88] or phenytoin,[89]resolves in the children whose medication is discontinued but persists in those maintained on this medication. The brain regions commonly involved in various types of epilepsies, such as the hippocampus and amygdala in temporal lobe epilepsy and subcortical nuclei in idiopathic generalized epilepsies, are important components of current models of depression.[89,90]

One study also found a sex effect with more depression in adolescent girls with epilepsy,[91] and another study noted an age effect with higher depression rates in adolescents. In contrast to depression with a trend in older children with epilepsy, anxiety is more comorbid in younger children (< 12 years old) with epilepsy.Certain psychiatric disorders, including primary mood disorders, increase the risk for suicide in adults with epilepsy. Only a few studies, however, examined suicidality in children with epilepsy.[83,87] Ott et al[83] reported suicidal ideation in 17% and 18% and suicidal intent in 8% and 11% of complex partial seizure and childhood absence epilepsy, respectively, but these rates were not significantly higher than those in normal children (9% ideation, 1% intent). Brent *et al*[87] found suicidal ideation in 40% of children with epilepsy treated with phenobarbital, compared with only 4% of children with epilepsy treated with carbamazepine.

Among the new AEDs, topiramate and lamotrigine already list suicidality on their package inserts but lack the evidence of clinical trials in pediatric patients.[92]

Other neuropsychiatric problems

To compare with healthy children, oppositional defiant (13% vs. 2%) and tic disorders (9.4% vs. 2%) are more common but considerably less prevalent.[69] A significantly increased rate of tic disorders is evident among children with localization-related epilepsy, and a significantly increased rate of conduct disorders in children with primary generalized epilepsy.[69]

The incidence of psychosis appears to be rare in children who have epilepsy. Ictal and postictal psychosis can occur but are rare.[70] A postictal psychotic episode may occur after a prolonged seizure or a cluster of seizures. The psychotic episode can last several days

and typically resolves spontaneously. If psychotic symptoms occur during seizures, they typically are stereotyped, and children may be unable to recall the content of the hallucination. This pattern is in contrast to children who have psychosis, who generally are able to describe the hallucination, which can vary from episode to episode. Changes in AEDs always should be considered when evaluating psychosis in children who have epilepsy. AED-induced psychotic reactions have been reported with the following medications: phenytoin, topiramate, lamotrigine, ethosuximide, vigabatrin, zonisamide, and felbamate.[68]

2. LITERATURE REVIEW

Lauren C[93] *et al.*, (2018)

They conducted a systemic review of qualitative studies to access the children's Experiences of Epilepsy. Forty-three articles involving 951 participants aged 3 to 21 years across 21 countries were included. We identified 6 themes: loss of bodily control (being overtaken, susceptibility to physical harm, fragility of the brain, alertness to mortality, incapacitating fatigue), loss of privacy (declarative disease, humiliating involuntary function, unwanted special attention, social embarrassment of medicine-taking), inescapable inferiority and discrimination (vulnerability to prejudice, inability to achieve academically, consciousness of abnormality, parental shame, limiting social freedom), therapeutic burden and futility (unattainable closure, financial burden, overwhelming life disruption, exhaustion from trialing therapies, insurmountable side effects, awaiting a fabled remission), navigating health care (empowerment through information, valuing empathetic and responsive care, unexpected necessity of transition, fragmented and inconsistent care), and recontextualizing to regain normality (distinguishing disease from identity, taking ownership, gaining perspective and maturity, social and spiritual connectedness).And this study was concluded stating children with epilepsy experience vulnerability, disempowerment, and discrimination. Repeated treatment failure can raise doubt about the attainment of remission. Addressing stigma, future independence, and fear of death may improve the overall well-being of children with epilepsy.

Anita C[94]*et al.*, (2018)

They conducted a study which aimed to assess the prevalence of Attention Deficit Hyperactivity Disorder (ADHD) and its characteristics and risk factors in children with epilepsy at a tertiary medical center in New Delhi. Children with active epilepsy, aged 6 to 12 years, were assessed for ADHD using DSM-IV-TR criteria. Epilepsy and psychiatric characteristics, sociodemographic indicators, and use of antiepileptic drugs were analyzed for differences between the ADHD and non-ADHD groups. Among the 73 children with epilepsy, 23% (n = 17) had comorbid ADHD, of whom 59% (n = 10) had predominantly inattentive type, 35% (n = 6) combined type, and 6% (n = 1) predominantly hyperactive-impulsive type. Lower IQ scores, epileptiform EEG activity, not attending school, and male sex were significantly associated with comorbid ADHD in children with epilepsy. Groups were similar in terms of age, socioeconomic indicators, family history of psychiatric disorders, seizure frequency in the last six months, seizure etiology, and seizure type. They concluded stating that epilepsy is a common pediatric neurological condition with frequent psychiatric comorbidities, including ADHD. Specialists should collaborate to optimize treatment for children with epilepsy and ADHD, especially for families in developing countries where the burden of disease can be great.

Bilgic A[95]*et al.*, (2018)

Conducted a regression analysis study in order to evaluate the psychiatric symptoms and health-related quality of life (HRQL) of children with epilepsy and psychiatric symptoms of their mothers, and compared them to those of healthy children and their mothers. This study also explored the influence of the child-related and maternal psychiatric variables

and seizure-specific factors on the HRQLs of children with epilepsy according to both the children's and parents' perspectives. Ninety-nine children with epilepsy (8 to 17years old), their mothers, and a control group (n=51) had participated in this study. The depression and anxiety symptoms of the children were assessed using the Child Depression Inventory (CDI) and the Screen for Child Anxiety-Related Emotional Disorders (SCARED), respectively. The severities of the attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder (CD) symptoms were assessed via the mother-rated Turgay DSM-IV-Based Child and Adolescent Behavioural Disorders Screening and Rating Scale (T-DSM-IV-S). In addition, the mothers completed the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) to assess their depression and anxiety symptoms, respectively. Child-reported and parent-reported Paediatric Quality of Life Inventories were used to evaluate the HRQLs of the children. The patients exhibited higher inattention and ODD scores than the controls did. With the exception of the child-reported physical health scores, all of the child- and parent-reported HRQL scores were significantly lower in the patient group. According to the regression analysis, the child-related psychiatric and seizure-specific factors, but not the maternal psychiatric factors, were associated with the child's HRQL. They concluded the study with the note that Epilepsy is associated with a poor psychiatric status and HRQL in childhood. The impact of epilepsy on the HRQL occurs mainly through child-related psychiatric factors. Both the child-reported and parent-reported questionnaires seem to be useful for the evaluation of the HRQL in paediatric epilepsy cases.

Dipika B[96]*et al.*, (2017)

They conducted a cross-sectional study of 256 children with epilepsy aged between 5 and 18 years on antiepileptic drug (AED) treatment for at least 3 months was performed and 125 age and sex matched healthy children were included. A generic version of the Pediatric Quality of Life (PedsQL version 4) scale was used to assess HRQOL. And it was noted that childrens with epilepsy had diminished scores in total score and all subdomains of PedsQL as compared to healthy children, children with epilepsy on polytherapy had diminished HRQOL compared with those on monotherapy, children with generalized seizures or with symptomatic epilepsy had diminished HRQOL. Significant predictors of poor HRQOL were adverse drug reactions (ADRs) to AED, polytherapy, longer duration of epilepsy, shorter seizure-free interval, and seizure frequency. Hence this study marked childrens with epilepsy have diminished HRQOL than healthy children in all subdomains of PedsQL. Significant predictors are ADRs to AED, polytherapy, longer duration of epilepsy, shorter seizure-free interval, and seizure frequency and comprehensive management of children with epilepsy must go beyond seizure control.

Hee-Yeon C[97]*et al.*, (2016)

They conducted a study to investigate the impact of specific behavioral problems on the health-related quality of life (HRQOL) in children and adolescents with epilepsy. Children and adolescents with epilepsy (n=92; age range=6–17 years) and their mothers had to complete questionnaires about behavioral problems, HRQOL, socio-demographics, and epilepsy-related variables. Inorder to determine significant predictor variables of the HRQOL, stepwise regression analyses and partial correlations were performed to adjust for other behavioral problems and covariates. The analyses revealed that an increase in

social behavioral problems and delinquent behaviour was associated with a decrease in the HRQOL. Lower levels of maternal education and the number of antiepileptic drugs were also associated with a decline in the HRQOL; the HRQOL and social behavioral problems remained significantly correlated after adjusting for maternal education level, number of antiepileptic drugs, and non-social behavioural problems. They concluded the study stating that parents and practitioners should be provided intervention if behavioral problems, particularly social behavioral problems, are observed in children or adolescents with epilepsy.

Dora N[98] *et al.*, (2014)

They conducted a cross sectional study in Indonesia to compare behavioral disorders in children with epilepsy to those in normal children, and to assess for possible factors associated with the occurrence of behavioral disorders. The study involved 47 children with epilepsy and 46 children without epilepsy, aged 3-16 years. Behavioral problems were screened with the Strength and Difficulty Questionnaire (SDQ), Indonesian version. Information about EEG description, medication, onset, and duration of epilepsy were obtained from medical records. Behavioral problems were found in 19.1% of children with epilepsy and only in 2.2 % of children without epilepsy (PR 8.8; 95%CI 1.16 to 66.77; P= 0.015). Significant differences were also found in the percentage of conduct problems and emotional disorders. Multivariate analysis with logistic regression revealed that the factors associated with behavioral disorders in children with epilepsy were uncontrolled epilepsy (PR 13.9; 95%CI 1.45 to 132.4; P=0.023) and focal EEG appearance (PR 19; 95%CI 1.71 to 214.43; P=0.017). It was also found that uncontrolled epilepsy was a factor related to emotional (PR 6.7; 95%CI 1.66 to 26.76; P=0.007) and

conduct problems (PR 6.1; 95%CI 1.35 to 27.29;P=0.019).Finally they stated that Uncontrolled epilepsy and focal EEG results are the factors associated with increased risk of behavioral problems in children with epilepsy. Children with epilepsy should undergo behavioral disorder screening, followed by diagnosis confirmation and treatment.

Mark A[99] *et al.*, (2014)

The aims of this study were to conduct a meta-analysis of risk factors for health-related quality of life (HRQL) in children with epilepsy; interpret the results in terms of study quality; and, assess the nature and source of heterogeneity of estimates. For this study databases were searched for studies that examined HRQL in pediatric epilepsy. The inclusion criteria were original studies published in English from 1994 through to the end of January 2014; children ≤18 years of age with epilepsy; included a parent- or self-reported measure of HRQL; and, data were presented such that the calculation of a correlation coefficient was possible. Study quality was measured using a modified Quality Index. A total of 12 risk factors from 21 studies were analyzed. The mean Quality Index score was 10.4 (standard deviation [SD] 1.9). Correlations between risk factors and HRQL had a minimum of r = −0.03 and a maximum of r = −0.44. Child sex, age, and age at onset were not significantly associated with HRQL. Duration of epilepsy, seizure type, frequency, and severity, number of antiepileptic drugs, side effects of antiepileptic drugs, presence of a comorbidity, parental anxiety, and family socioeconomic status were significantly associated with HRQL. Informant (child vs. parent), year of publication, and study quality were found to be sources of heterogeneity for certain risk factors. The result of this study demonstrated that a variety of clinical and family factors are associated with HRQL in children with epilepsy and have implications for research and practice.

Edwin E[100]*et al.*, (2013)

The objective of this study was to identify caregiver challenges in the provision of care to children with epilepsy presenting in a psychiatric unit. Administration of a structured questionnaire to caregivers of children with epilepsy presenting, between September and December 2011, in the newly constituted Child and Adolescent Mental Health(CAMH) Unit of the Federal NeuroPsychiatric Hospital, Kaduna Nigeria. A total of 84 caregivers were interviewed. The age range of the caregivers was 23 to 62 years (mean 38 ± 9.2 years) and a female preponderance (50, 59.5%). Most of the caregivers were in the upper social classes (I-III, 79.8%). A high number of challenges were indicated by majority 65, 77.4%) of the caregivers. The recurrence of seizures (84,100%) was the commonest challenge while the experience of discrimination (17, 20.2%) was the least. All caregivers had sought remedy from multiple health care options. Challenges were significantly ($P < 0.05$) associated with the female caregiver, age < 40 years, generalized type of epilepsy and residing outside Kaduna. This study identified multi dimensional caregiver challenges and highlighted the need for provision of comprehensive health and social services to children with epilepsy and their families.

Zeinab M[101]*et al.*, (2013)

They conducted a cross sectional study in Egypt to assess the health-related quality of life and its predictors in children with epilepsy, comparing the relationship between different types of seizures and health-related quality of life. The study included 50 epileptic children aged 8-12 years, with a mean age of 9.35 ± 1.59 years and a male to female ratio of 1.8:1. They were divided into two subgroups according to the types of seizures: 26 patients with generalized seizures in subgroup I and 24 patients with partial

seizures in subgroup II, and 50 apparently healthy children of matched age, sex, and social class were included as the control group. The Arabic version of the 23-item Pediatric quality of life Generic Core Scale (Parents' scale) was applied to evaluate the health-related quality of life of both patients and healthy controls. Highly significant lower overall quality of life scores of all functioning domains of health-related quality of life were present between patients' subgroups ($P < 0.001$), and between total patients versus control groups ($P < 0.001$). Univariate analysis was performed to identify significant predictors of poorer quality of life in children with epilepsy. On analyzing the risk factors using odds ratio, epilepsy-related risk factors such as age at onset of seizures, types of seizures, duration of the illness, number and duration of antiepileptic drugs as well as children's clinical variables such as learning problems, developmental delay in milestones, limitation in child hobbies, urine incontinence, and prolonged sleep, and some family-related variables such as marital disharmony and parental anxiety were found to be significantly strong predictors of poorer health-related quality of life in children with epilepsy, with prediction of 95%.

Shirley A[102] *et al.*, (2012)

They conducted a study to determine sociodemographics, patterns of comorbidity, and function of US children with reported epilepsy/seizure disorder. Bivariate and multivariable cross-sectional analysis of data from the National Survey of Children's Health (2007) on 91 605 children ages birth to 17 years, including 977 children reported by their parents to have been diagnosed with epilepsy/seizure disorder. Estimated lifetime prevalence of epilepsy/seizure disorder was 10.2/1000 (95% confidence interval [CI]: 8.7–11.8) or 1%, and of current reported epilepsy/seizure disorder was 6.3/1000 (95% CI:

4.9–7.8). Epilepsy/seizure disorder prevalence was higher in lower-income families and in older, male children. Children with current reported epilepsy/seizure disorder were significantly more likely than those never diagnosed to experience depression (8% vs 2%), anxiety (17% vs 3%), attention-deficit/hyperactivity disorder (23% vs 6%), conduct problems (16% vs 3%), developmental delay (51% vs 3%), autism/autism spectrum disorder (16% vs 1%), and headaches (14% vs 5%) (all $P < .05$). They also had greater risk of limitation in ability to do things (relative risk: 9.22; 95% CI: 7.56–11.24), repeating a school grade (relative risk: 2.59; CI: 1.52–4.40), poorer social competence and greater parent aggravation, and were at increased risk of having unmet medical and mental health needs. Children with prior but not current seizures largely had intermediate risk. They concluded the study stating that in a nationally representative sample, children with seizures were at increased risk for mental health, developmental, and physical comorbidities, increasing needs for care coordination and specialized services. Children with reported prior but not current seizures need further study to establish reasons for their higher than expected levels of reported functional limitations.

Thomas V[103] *et al.*, (2011)

The aim of the study was to identify the risk factors for epilepsy in children by using case–control retrospective study design in the pediatric neurology outpatient service of the Trivandrum Medical College. All children (1–12 years) with epilepsy satisfying the selection criteria were included, after obtaining consent from parents. Those with single seizures or febrile seizures were excluded. Controls were children without epilepsy attending the same hospital. Parents were interviewed and clinical data were obtained from medical records. Statistical analysis included chi-square test, odds ratio (OR), and

logistic regression.There were 82 cases and 160 controls whose mean age was 6.9 + 3.6 and 5.2 + 3.1, years respectively. On univariate analysis, family history of epilepsy, prolonged labor, cyanosis at birth, delayed cry after birth, admission to newborn intensive care unit, presence of congenital malformations, neurocutaneous markers, incessant cry in the first week, delayed developmental milestones, meningitis, encephalitis, and head trauma were found to be significant. On logistic regression, family history of epilepsy (OR 4.7), newborn distress (OR 8.6), delayed developmental milestones (OR 12.6), and head trauma (OR 5.8) were found to be significant predictors. Infants who had history of newborn distress are likely to manifest epilepsy before 1 year if they are eventually going to have epilepsy (OR 3.4).They concluded the study marking modifiable factors such as newborn distress and significant head trauma are significant risk factors for childhood epilepsy. Newborn distress is a risk factor for early-onset (<1 year age) epilepsy.

Ozalp E[104]*et al.*, (2009)

They conducted a review study to assess the prevalence of depression and anxiety among epilepsy patients. Among the psychiatric comorbid conditions in children and adolescents with epilepsy, depression and anxiety disorders require further attention because they carry the risk of reduced quality of life and life-threatening complications (e.g., suicide). Research in recent years has shed light on both the prevalence of emotional problems in youth with epilepsy and the safety and efficacy of treatment options. A number of challenges exist in treating patients with epilepsy. This is particularly true when seizures are difficult to control and medication regimens are more complex. Some pharmaceutical options may provide assistance with both seizures and emotional distress, but care is needed when considering such treatment approaches. In addition, integration of mental

health professionals into the care of patients is necessary when cases are complicated and risk factors are high. Thorough methods to accurately diagnose emotional conditions and regular monitoring of symptoms can help prevent serious problems that can negatively affect the success of children and adolescents in everyday life. Collaboration between disciplines offers the best hope for early identification and treatment of these conditions

Lagunju I[105]*et al.*, (2009)

They conducted a study to assess the HRQOL of Nigerian children with epilepsy and the psychosocial impact of the disease on the parents of affected children. A standardized questionnaire adapted from the PedsQL Questionnaire was applied to evaluate the HRQOL in 66 consecutive children with epilepsy, aged ≥5 years seen at the University College Hospital, Ibadan during a 3 month period. A total of twenty children (30.3%) showed significant impairment in the HRQOL with the major impact found in the areas of general health, family life, school activity and self esteem. There was a statistically significant association between seizure severity, parental emotional impact, maternal level of education and impaired HRQOL. They concluded the study stating that Impaired HRQOL is a major issue in Nigerian children with epilepsy. The extended family support system does not appear to have any ameliorating effect on the stress experienced by the affected families. This study suggests the need for psychosocial support to achieve optimal care for children on antiepileptic drugs.

Prahbhjot M[106]*et al.*, (2005)

Conducted a study to examine the quality of life of children with epilepsy and to identify the demographic, disease related, and behavioral and emotional functioning variables in the prediction of quality of life of children with epilepsy.Forty three children aged 4 to 15

years (Mean=10.3 years) with epilepsy were recruited from the outpatient services of the Department of Pediatrics, of a tertiary care teaching hospital in North India. Quality of life was measured by Impact of Epilepsy Schedule, a 39 items parent reported questionnaire and child's emotional and behavioral functioning at home was assessed by the Childhood Psychopathology Measurement Schedule.Majority of the parents expressed major concerns regarding seizures, treatment by anticonvulsants, present and future problems for the child and problems in parenting. Nearly 40% of the children had psychopathology scores in the clinically significant maladjustment range. Step-wise multiple regression analysis revealed that the psychopathology scores and mother's education accounted for 39% of the variance in the quality of life scores. They concluded the study noting that children with epilepsy have a relatively compromised quality of life and focusing simply on control of seizures may not address the full range of child's emotional and behavioral difficulties.

Gabriel M[107] *et al.*, (2003)

They conducted a study by combining qualitative and quantitative research methods. Items were extracted from focus group discussions involving children with epilepsy and their parents. The main objective of the study was to answer a need to include and measure accurately the impact and burden of epilepsy as outcomes of interventions with affected children. A sample of 381 children with epilepsy, age 6–15 years, and their parents independently completed a 67-item questionnaire, from which they have chosen five items for each sub- scale. They concluded the study stating that the data demonstrate sound psychometric properties for both related measures, which are easy to administer for children with epilepsy who are 8 years and older and their parents. The subscales

encompass HRQL dimensions judged most important by children with epilepsy for the self-report measure and by parents for the proxy response measure. The parent-proxy measure should be useful as a complement to the child self-report measure in evaluating the validity of parental assessment of the child's health status; in longitudinal outcome research; and in HRQL assessment of children who are unable to respond independently.

3. AIM AND OBJECTIVES

Epilepsy is one of the most common chronic neurologic conditions in children, and it is associated with increased risk for poor health related quality of life.[108,109] Children with epilepsy experience difficulty in aspects of functioning, including emotional and behavioral problems, Social competence, academic achievement, and family life, with effects extending into adulthood.[110,111]The management of epilepsy requires recognition of potential effects of epilepsy and all aspects of life.[112] Childhood epilepsy is one of the most significant and prevalent neurological condition in the developing years. Several studies indicate that childhood epilepsy is a high risk factor for poor psychosocial outcomes including depression and anxiety,[113] low self-esteem,[114-116]behavioral problems[117-119]and academic difficulties.[120]

Quality of life of Indian children is affected by age, seizure frequency, parent's education, type of epilepsy, and type of anti epileptic drug prescribed. Cognition, energy levels and concentration are most commonly affected due to epilepsy.[121] QOL can be assessed by generic or disease specific measures. Generic measures of QOL assess function, disability and distress resulting from general ill health and have the advantages of allowing comparisons with healthy population.[122,123] Quality of life (QOL) is concerned with the degree to which a person enjoys the important possibilities of life". Health-related quality of life (HRQOL) characterizes a person's perception of how health influences an individual's life quality and overall well-being. Quality of life is an important measurable outcome of care for conditions that do not threaten life.[124] The generic scales used to measure the QOL like child health questionnaire are insufficiently sensitive to epilepsy.[125] There is lack of research on QOL among children with epilepsy from the developing

countries, with only a few studies from India.[126] We planned the present study to assess the QOL using Quality Of Life in Children with Epilepsy (QOLCE -55) questionnaire. Factors such as age at disease onset, seizure etiology, seizure type, epilepsy syndrome, comorbid conditions, and non-adherence to AEDs could lead to poor seizure control among epilepsy patients.

Aim

The aim of the study is explore the current status of Quality of Life (QOL) in epileptic children by using QOLCE-55 questionnaire.

Objectives

- To Study the Demographic profile of Children with Epilepsy
- To Study the Quality of Life (QOL) of Children with Epilepsy
- To study the association of Quality of Life (QOL) and socio demographic factors

4. METHODOLOGY

Epileptic patients recruited from the department of Pediatrics, at the tertiary care teaching hospital, Erode, India. It is a prospective observational study. The age of the children ranged from 4-15 years. Epileptic children receiving anti epileptics for at least a period of 6 months will be included in the study. The following demographic factors were recorded in perform a age, gender, parental education status, income and place of residence etc. Clinical factors were determined and recorded in terms of seizure type, seizure frequency over preceding 6 months, number of AEDs and duration of seizures. Patient's seizure type was classified broadly as generalized seizures, partial seizures and partial seizures with secondary generalization. Seizure frequency was determined as per the history recalled by parents. Socio-economic status was finally determined as per revised Kuppuswamy classification.[127]

Quality of Life (QOL) in epileptic children studied using QOLCE-55 questionnaire. Patient response from past and present medical and medication history and by referring the case sheets and by interacting with the patient and patient care taker by using questionnaire.

The QOLCE will be filled and coded by as per the standard instructions available with the questionnaire. QOLCE consists of 4 subscales. Each subscale has number of items or questions with responses as excellent, very good, good, fair, and poor. They are changed to 1, 2, 3, 4 and 5 as per instructions. Ten changed on a scale of 100 i.e., 1=0, 2=25, 3=50,4=75, 5=100. Items corresponding to each subscale are marked and their mean score is score of that subscale. An overall QOL score will be computed by adding each subscale score for each individual and then dividing by respective number of items. The

QOLCE-55 was translated into Tamil. Translation was done by two qualified independent translators; both native speakers of Tamil and proficient in English. It was retranslated to English and found to be similar. The final version of Tamil questionnaire was completed and made available for the reliability and validity study. It was validated by institutional committee members. The study was approved by institutional Ethical committee.

Inclusion criteria

Epilepsy was defined as presence of two or more unprovoked seizures. Children aged between 4 and 15 years with minimum duration of epilepsy of 6 months were the cases.

Exclusion criteria

Children with co-morbid neurodevelopment conditions (mental retardation, developmental delay, cerebral palsy, autism, Attention deficit hyperactivity disorder (ADHD) behavioral disorders, etc.) and chronic medical conditions (asthma, hypertension, chronic renal failure (CRF), chronic lung disease (CLD), thalassemia, hypothyroidism, etc.) were excluded. Children whose primary caregiver was not available to answer the questionnaire were also excluded.

Statistical analysis

The data were entered into Microsoft Excel and statistical analysis was performed using the SPSS 15.0 version (SPSS, Inc., Chicago, IL, USA). Categorical variables like demographic and clinical factors were expressed as numbers and proportions; whereas, QOL scores was expressed as mean and standard deviation.

5. RESULTS

Table 1:Distribution of epileptic patients according to gender

S.No.	Gender	Number of Children (n=113)	Percentage (%)
1	Male	59	52.21
2	Female	54	47.79

Figure 1:Distribution of epileptic patients according to gender

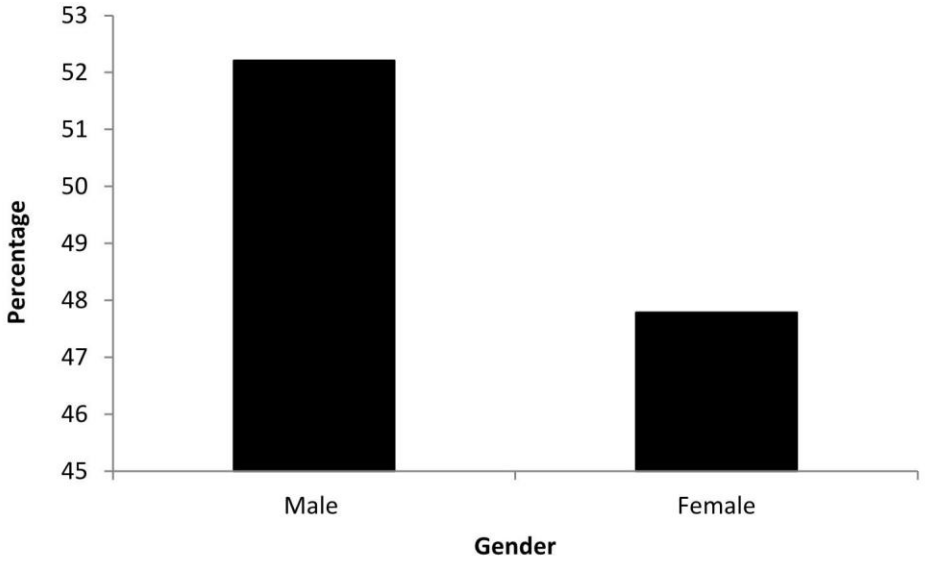


Table 2: Distribution of epileptic patients according to age

S.No.	Age (years)	Number of Children (n=103)	Percentage (%)
1	4 to 6	17	15.04
2	7 to 9	37	32.74
3	10 to 12	38	33.63
4	13 to 15	21	18.58

Figure2:Distribution of epileptic patients according to age

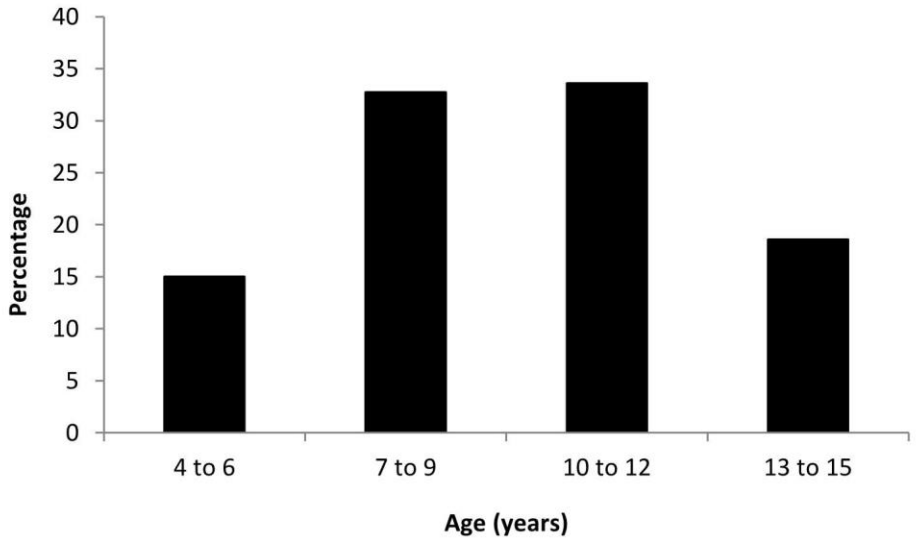


Table 3:Distribution of epileptic patients according to education

S.No	Educational level	Number of Children (n=103)	Percentage (%)
1	Kindergarden/ Nursery school	13	11.50
2	Elementary school/ Primary Schools	71	62.83
3	Middle Schools / Secondary (High) Schools	29	25.66

Figure 3:Distribution of epileptic patients according to education

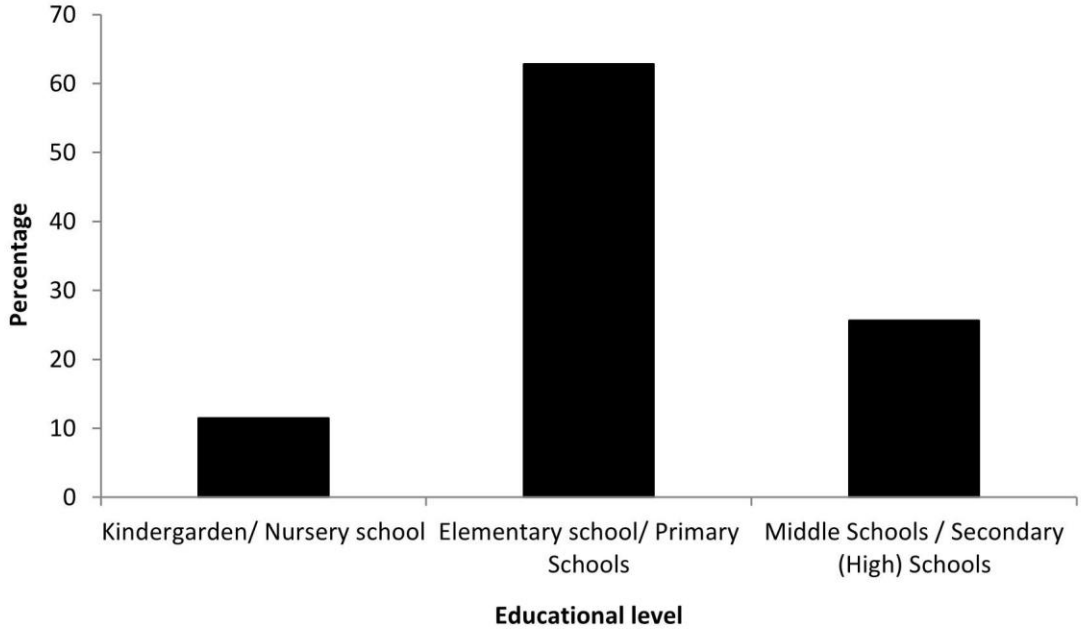


Table 4: Age of onset of Epilepsy

S.No	Age of onset	Number of patients (n=113)	Percentage (%)
1	0 to 3	41	36.28
2	4 to 6	33	29.20
3	7 to 9	23	20.35
4	10 to 12	11	9.73
5	13 to 15	2	1.77
6	No answer	3	2.65

Figure 4: Age of onset of Epilepsy

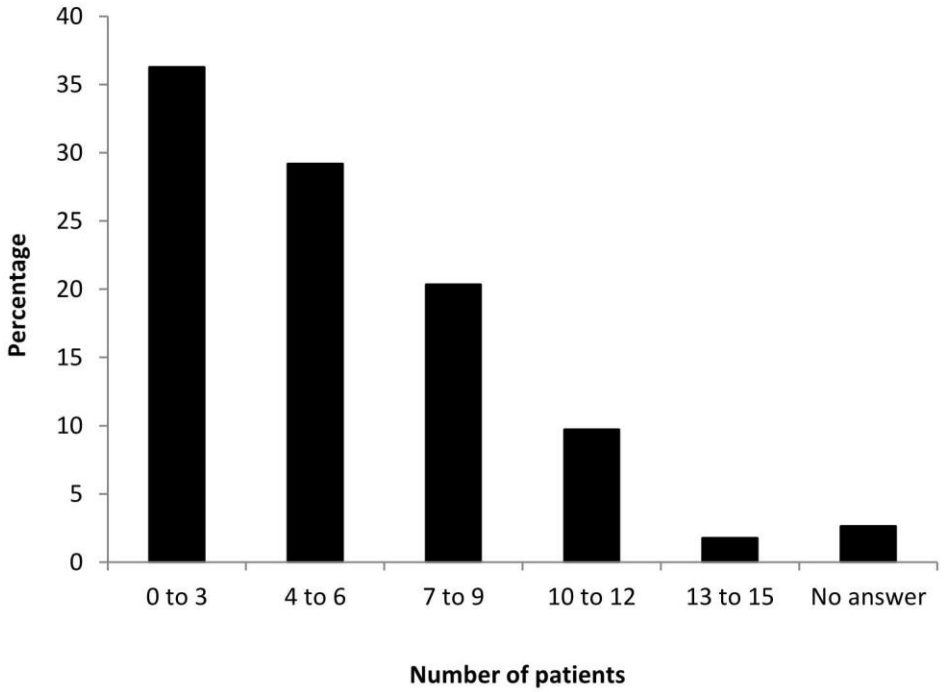


Table 5: Frequency of seizures in the past year

S.No	Frequency of seizures in the past year	Number of patients (n=113)	Percentage (%)
1	Almost daily	11	9.73
2	Once a week or more frequently	6	5.31
3	Several times a month	13	11.50
4	Several times a year	28	24.78
5	Not occurred	55	48.67

Figure 5: Frequency of seizures in the past year

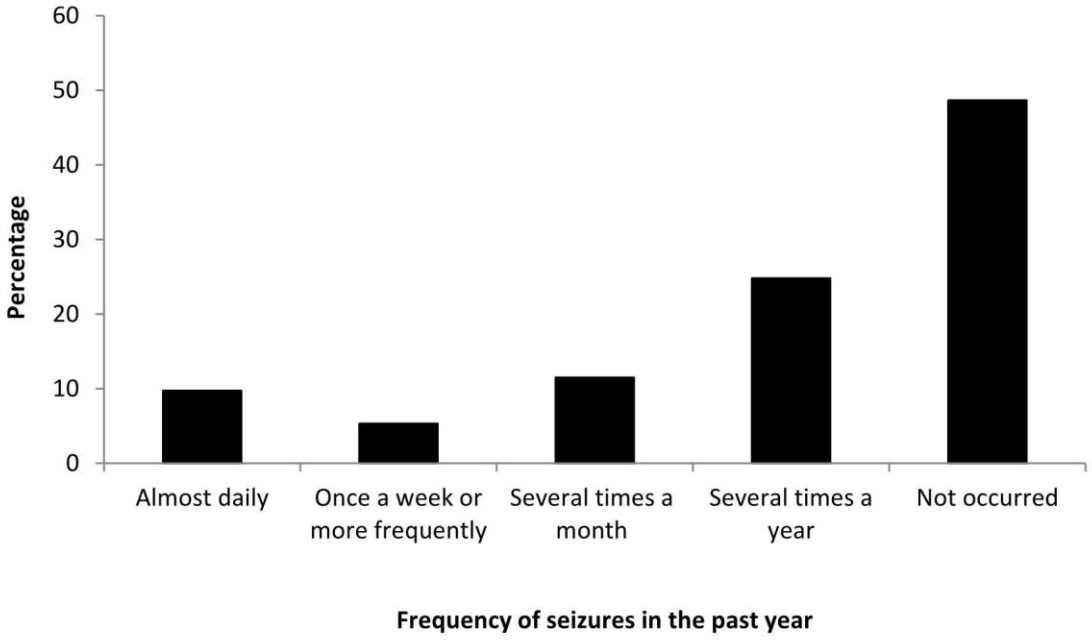


Table 6: Number of Anti Epileptic Drugs Prescribed

S.No	Number of AEDs	Number of patients (n=113)	Percentage (%)
1	No medications	5	4.42
2	1 medication	46	40.71
3	2 medications	54	47.79
4	3 medications	8	7.08

Figure 6:Number of Anti Epileptic Drugs Prescribed

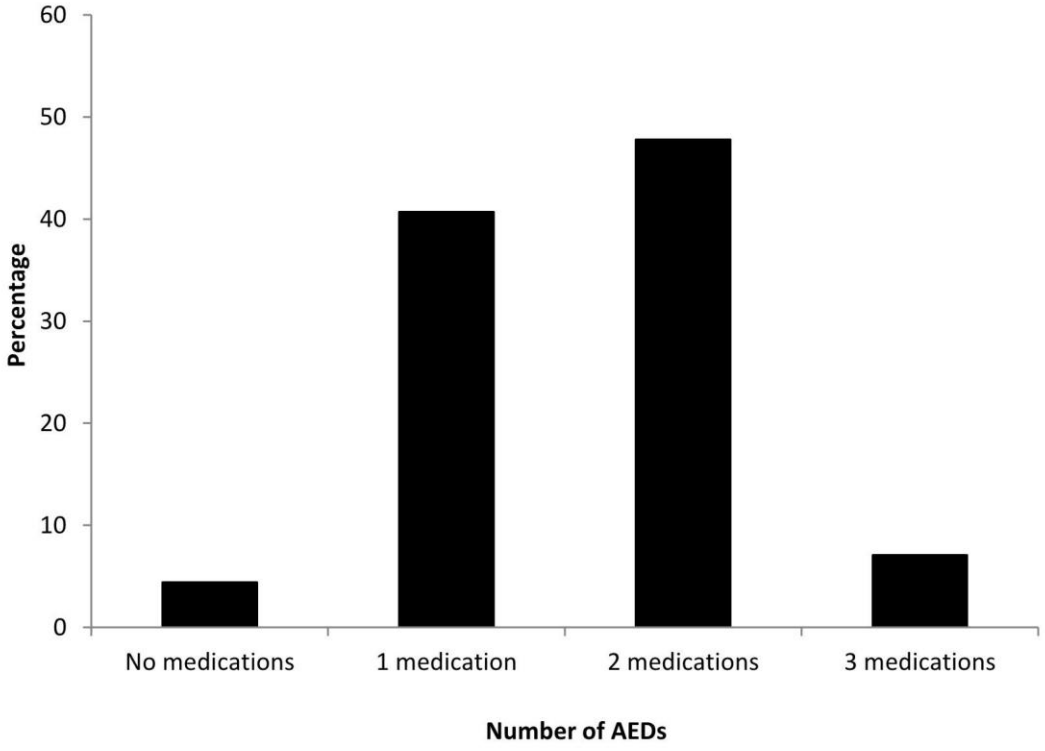


Table 7: Seizure Lateralization

S.No	Seizure Lateralization	Number of patients (n=113)	Percentage (%)
1	Left	45	39.82
2	Right	36	31.86
3	Bilateral	32	28.32

Figure7: Seizure Lateralization

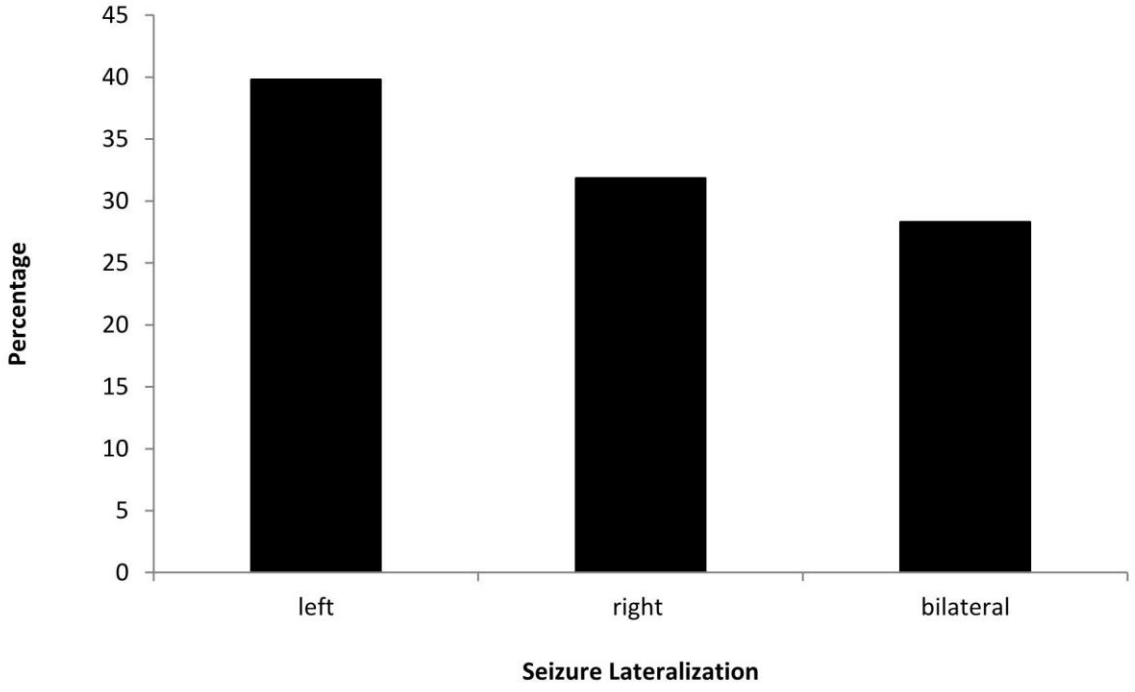


Table 8: Family history of epilepsy

S.No	Family history of epilepsy	Number of patients (n=113)	Percentage (%)
1	Present	13	11.50
2	Absent	100	88.50

Table 8: Family history of epilepsy

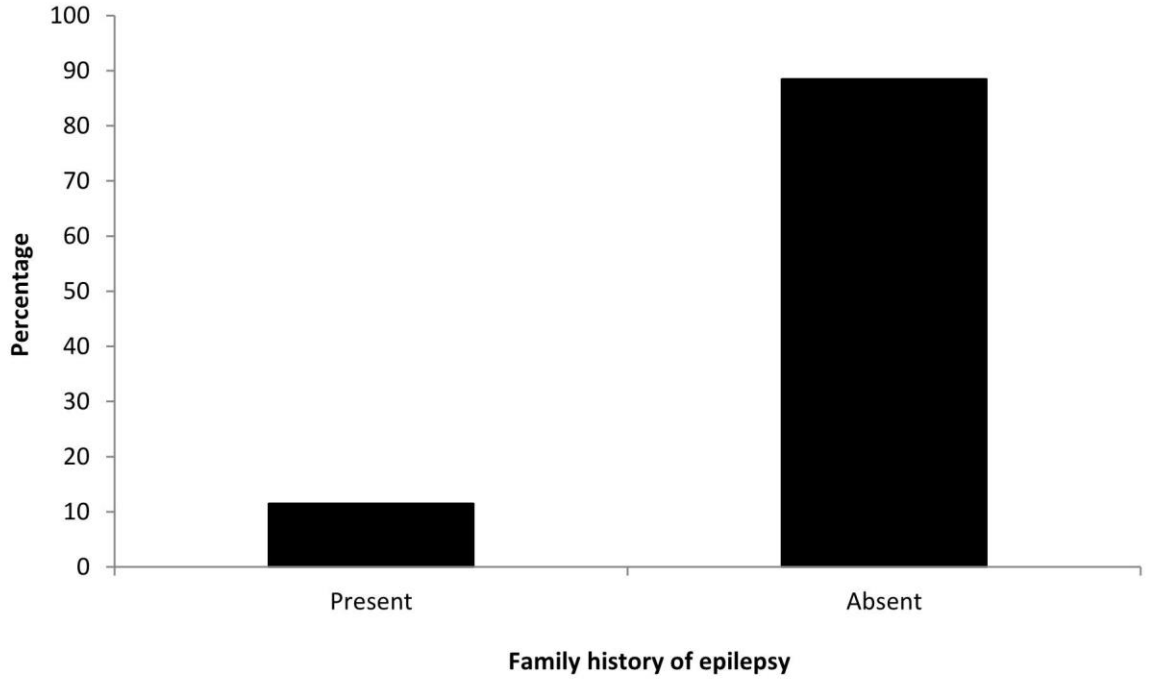


Table 9:Details of Microcephaly

S.No	Microcephaly	Number of patients (n=113)	Percentage (%)
1	Present	5	4.42
2	Absent	108	95.58

Figure9:Details of Microcephaly

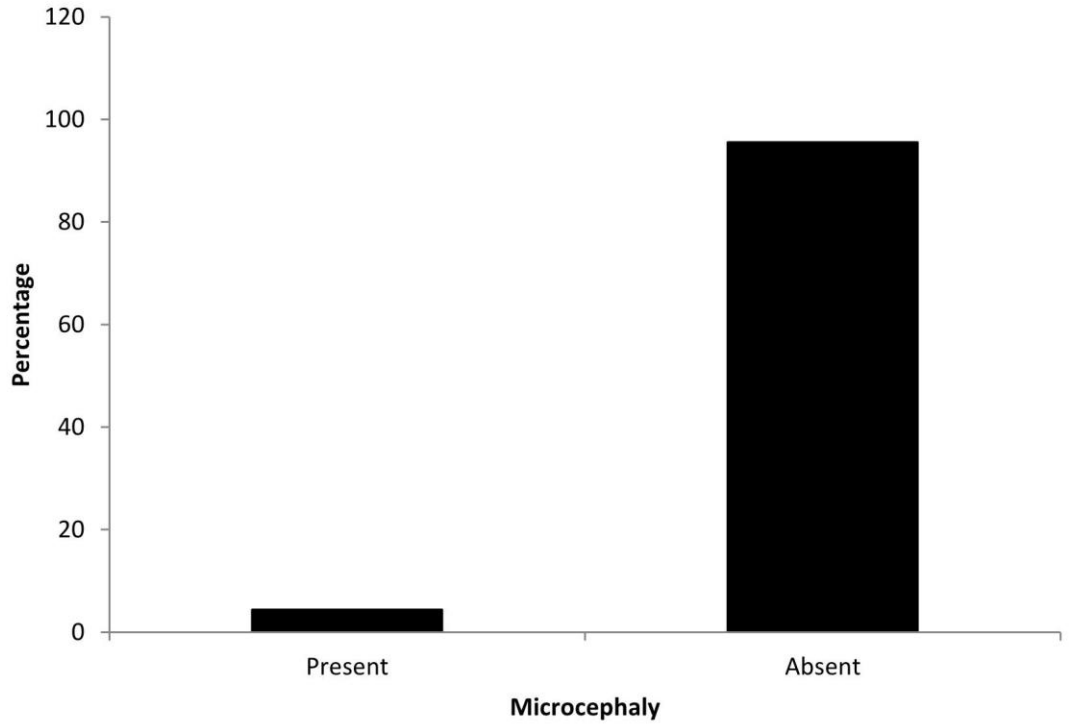


Table 10: Mother's educational Level

S.No	Mother's educational Level	Number of patients (n=113)	Percentage (%)
1	Iliterate	34	30.09
2	Until high school	62	54.87
3	Above high school	17	15.04

Figure 10: Mother's educational Level

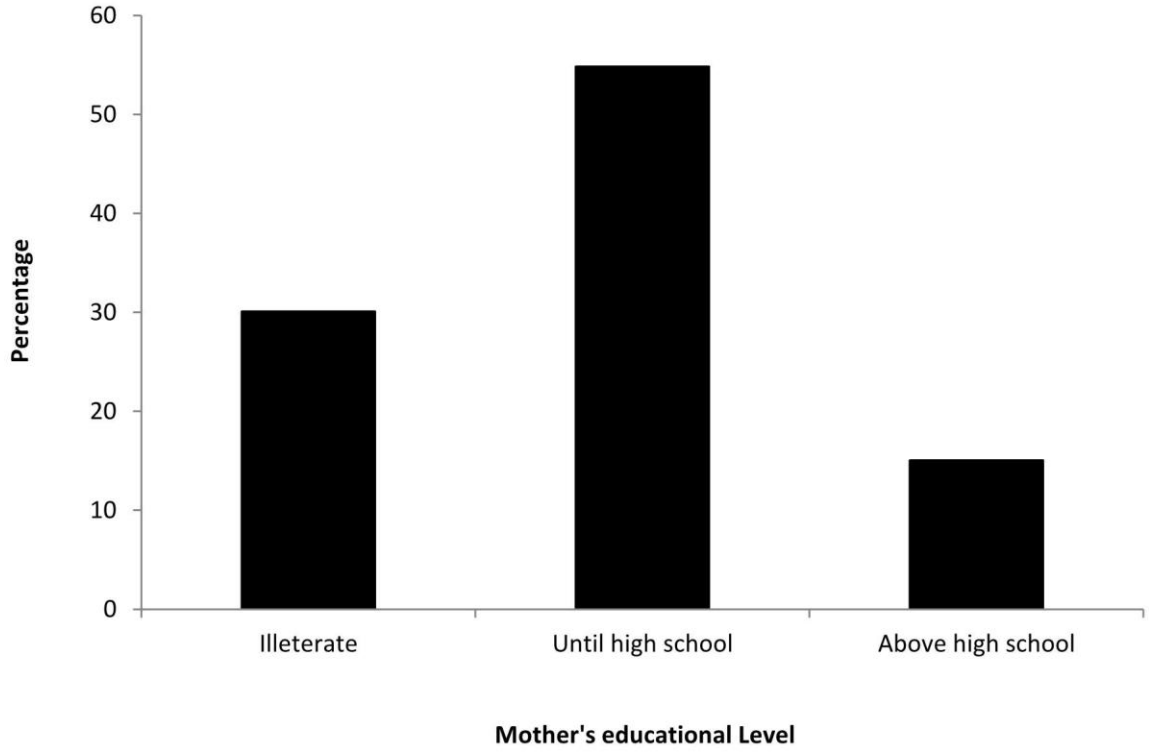


Table 11: Father's educational Level

S.No	Father's educational Level	Number of patients (n=113)	Percentage (%)
1	Iliterate	23	20.35
2	Until high school	56	49.56
3	Above high school	34	30.09

Figure11: Father's educational Level

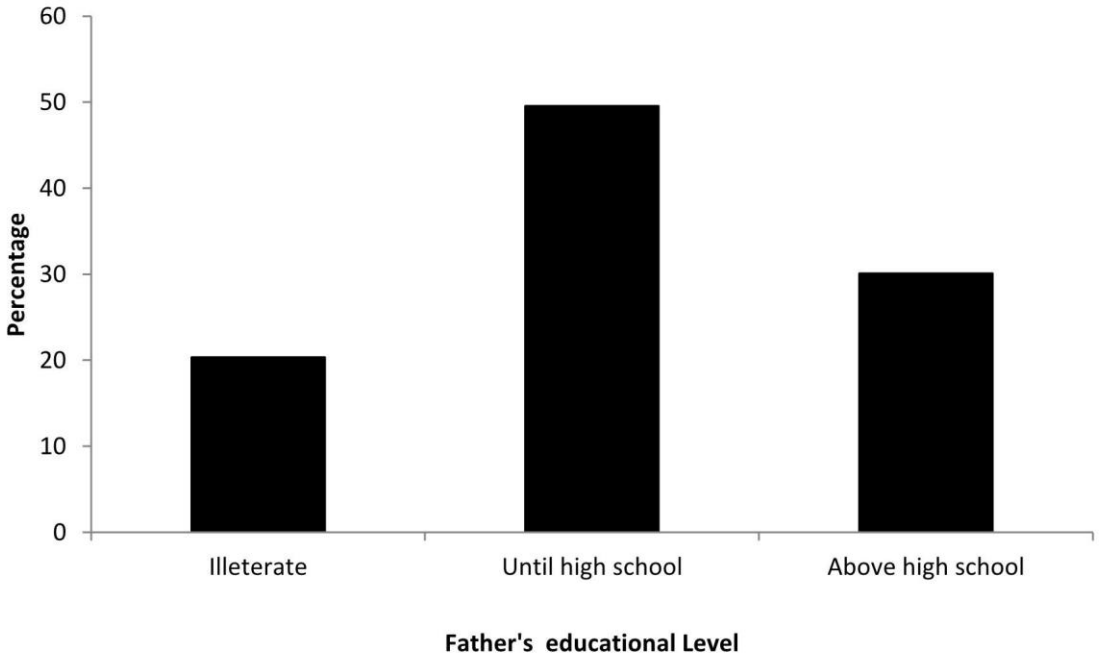


Table 12: Socio-economic status of parents

S.No	Socio-economic status	Number of patients (n=113)	Percentage (%)
1	Low	42	37.17
2	Middle	62	54.87
3	High	9	7.96

Figure12: Socio-economic status of parents

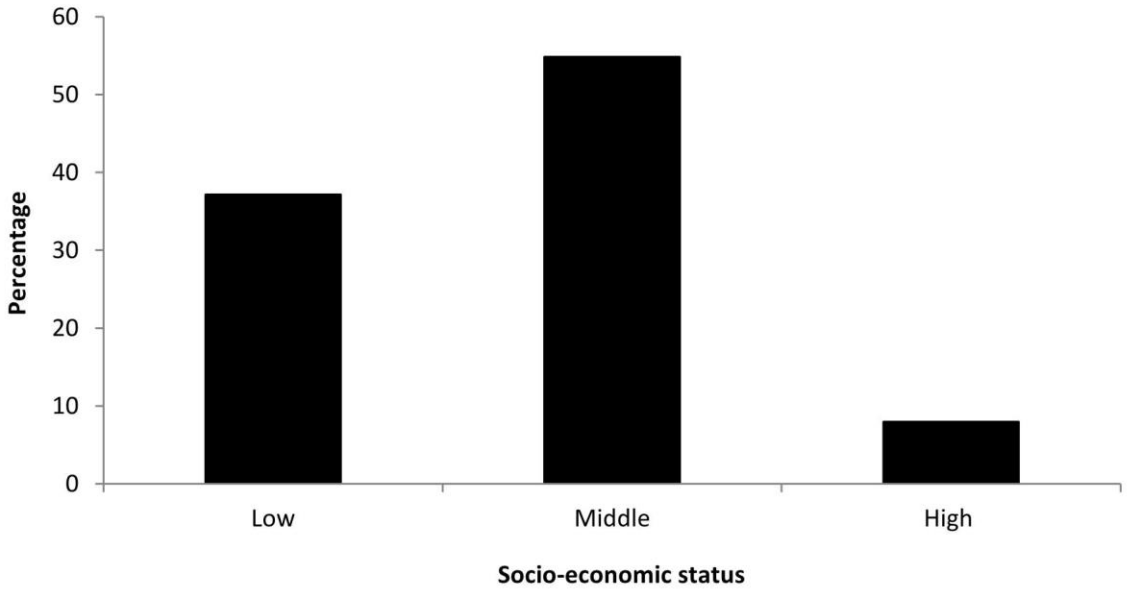


Table 13: Type of epilepsy

S.No	Type of epilepsy	Number of patients (N=113)	Percentage (%)
1	Generalized seizure	85	75.22
2	Partial	28	24.78

Figure 13: Type of epilepsy

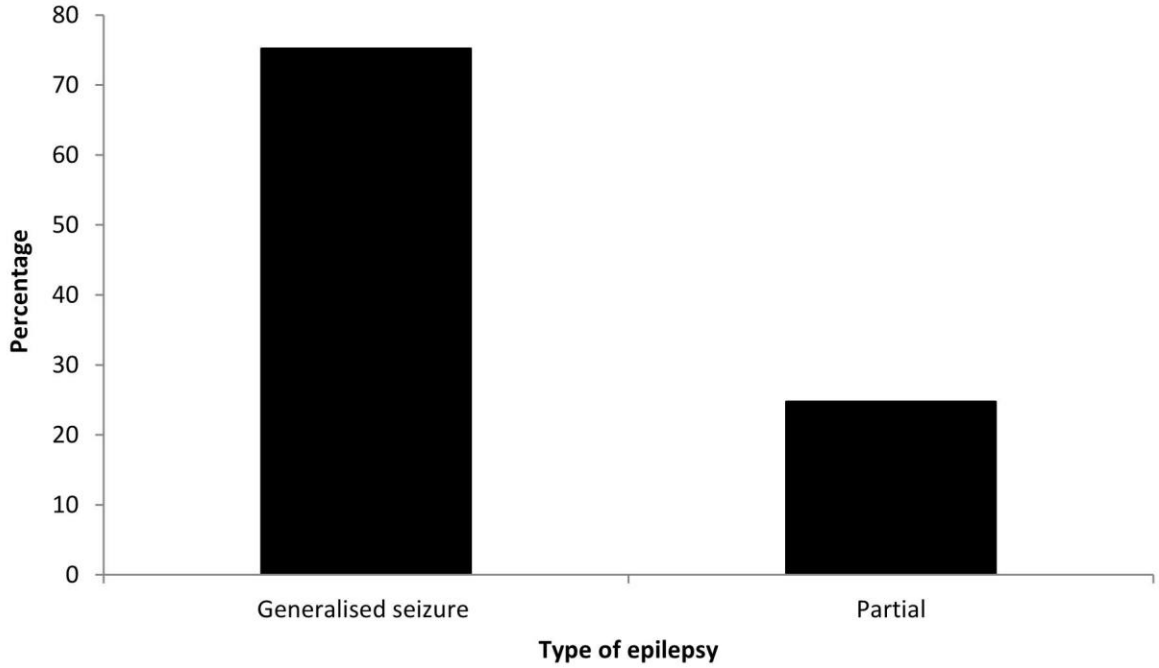


Table 14: Score of QOLCE-55 questionnaire

S.No	Scale	No. of items	QOLCE-55 Score (Mean)	SD
1	Cognitive functioning	31	43.72	14.12
2	Emotional functioning	23	57.81	8.92
3	Social functioning	17	55.67	15.01
4	Physical functioning	19	75.65	10.07

Figure14: Score of QOLCE-55 questionnaire

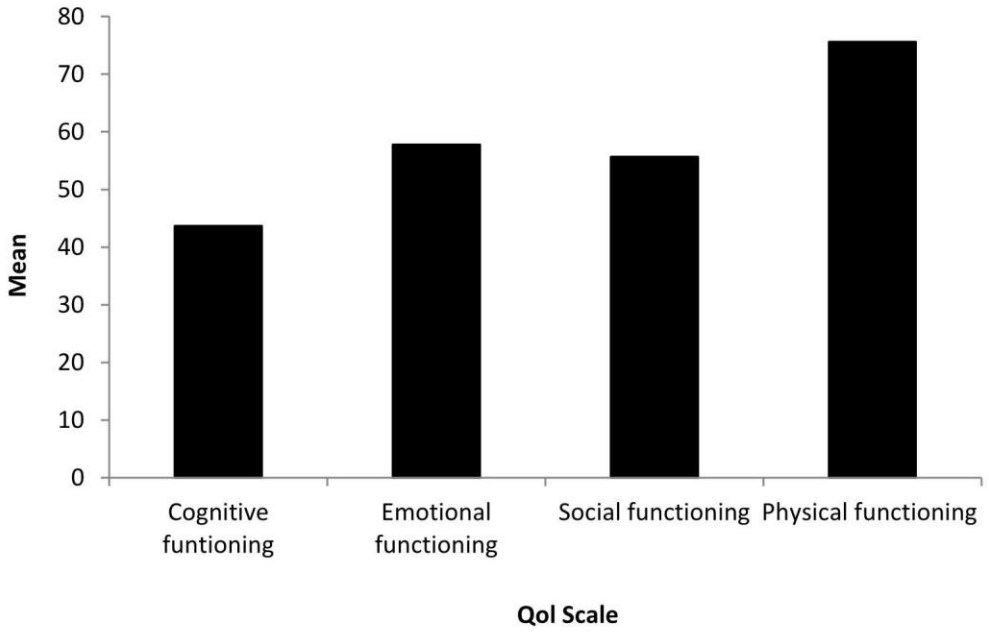


Table 15: Association of age and quality of life in children with epilepsy

S.No	Age in years	Overall QOL Mean	SD
1	4 to 6	63.5	2.91
2	7 to 9	64.5	3.84
3	10 to 12	62.8	2.72
4	13 to 15	66.2	5.23

Figure15: Association of age and quality of life in children with epilepsy

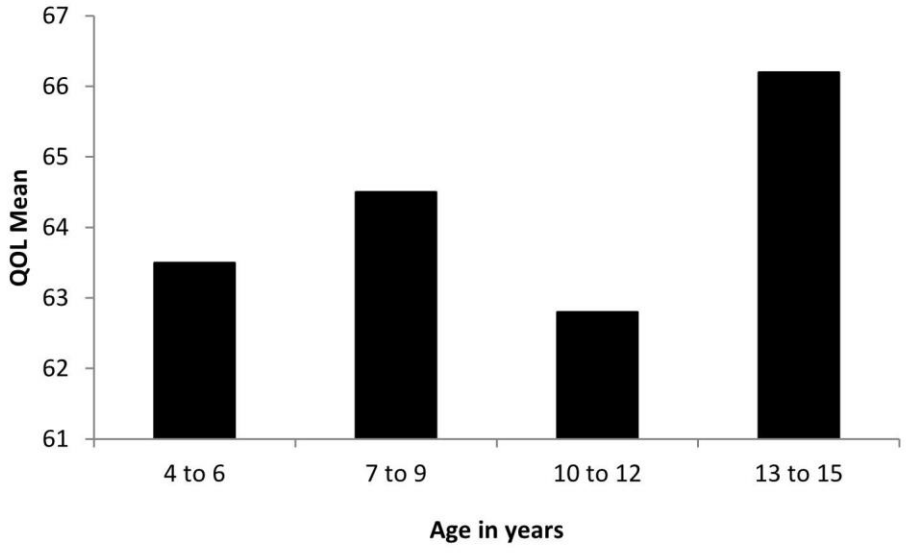


Table 16: Association of Gender and quality of life in children with epilepsy

S.No	Gender	Overall QOL Mean	SD
1	Male	62.2	4.21
2	Female	63.7	3.97

Figure16: Association of Gender and quality of life in children with epilepsy

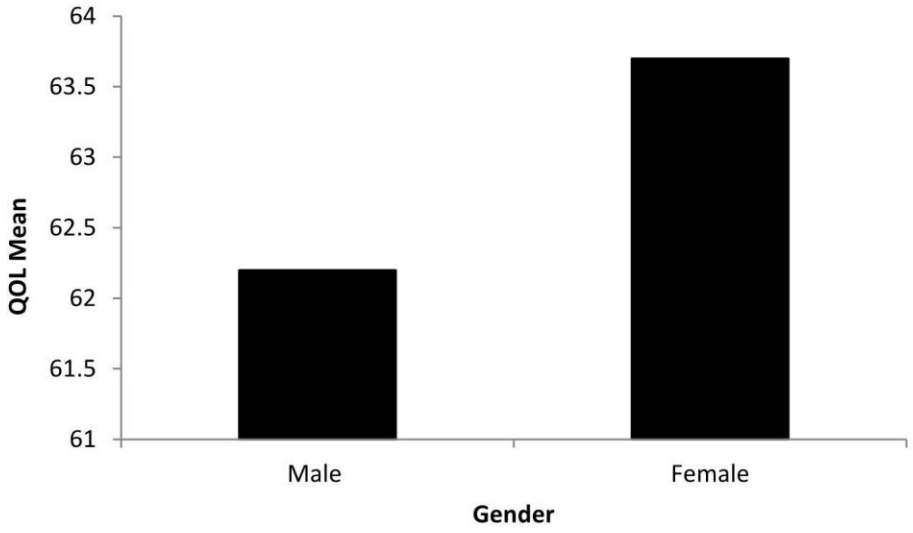


Table 17: Association of Mother's educational Level and quality of life in children with epilepsy

S.No	Mother's educational Level	Overall QOL Mean	SD
1	Iliterate	64.6	3.78
2	Until high school	64.5	4.72
3	Above high school	63.4	3.91

Figure17: Association of Mother's educational Level and quality of life in children with epilepsy

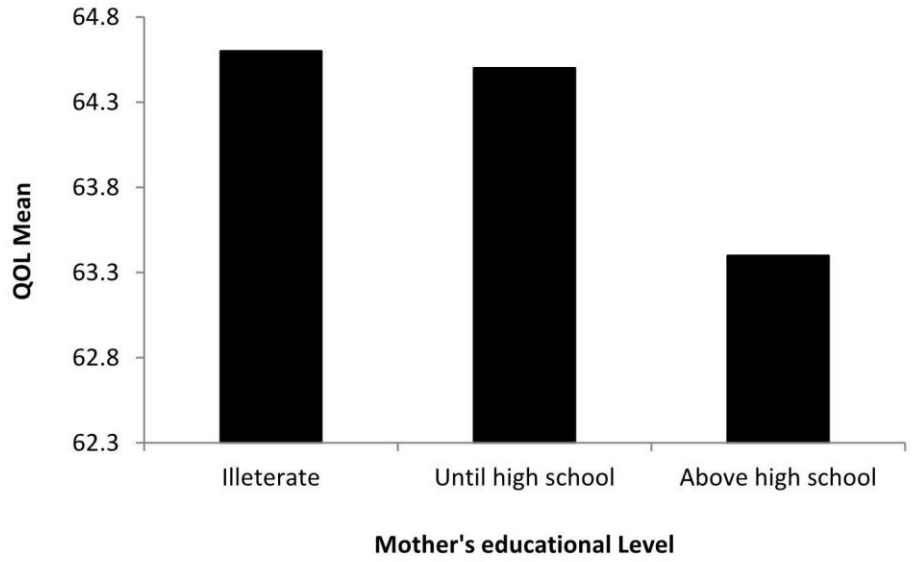


Table 18: Association of Mother's educational Level and quality of life in children with epilepsy

S.No	Father's educational Level	Overall QOL Mean	SD
1	Iliterate	65.4	4.21
2	Until high school	64.7	3.89
3	Above high school	64.3	3.87

Figure18: Association of Mother's educational Level and quality of life in children with epilepsy

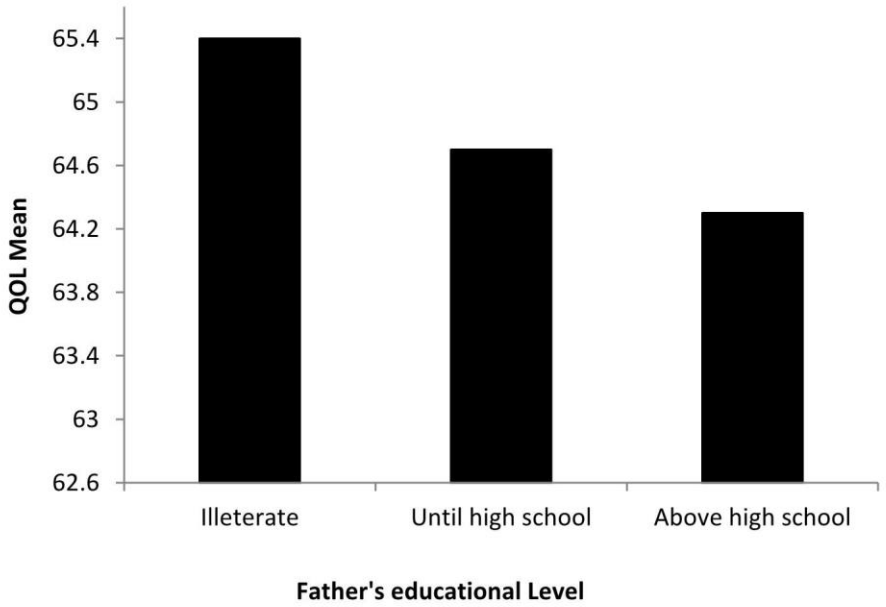


Table 19: Association of Socio-economic status and quality of life in children with epilepsy

S.No	Socio-economic status	Overall QOL Mean	SD
1	Low	64.5	3.72
2	Middle	64.6	3.43
3	High	65.5	4.54

Figure19: Association of Socio-economic status and quality of life in children with epilepsy

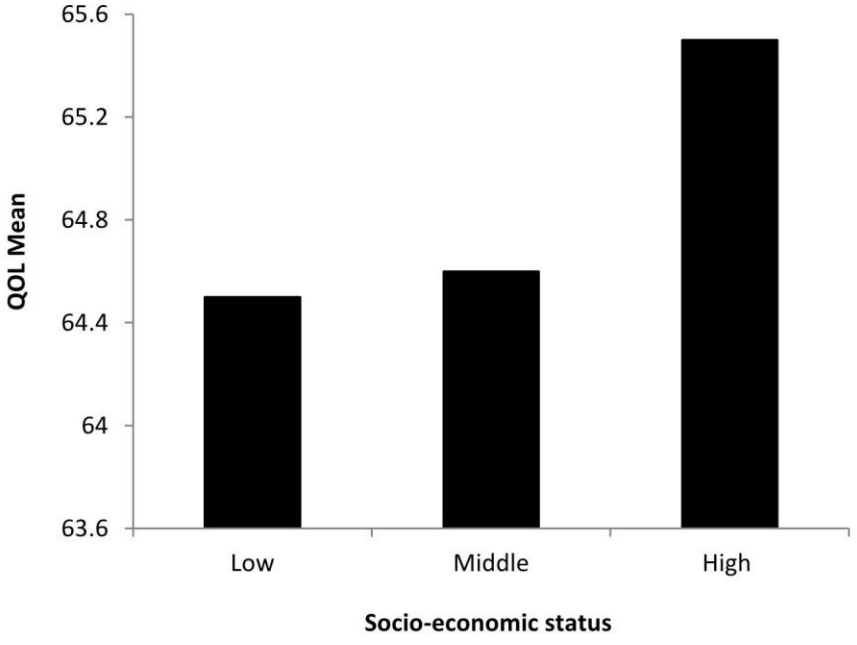
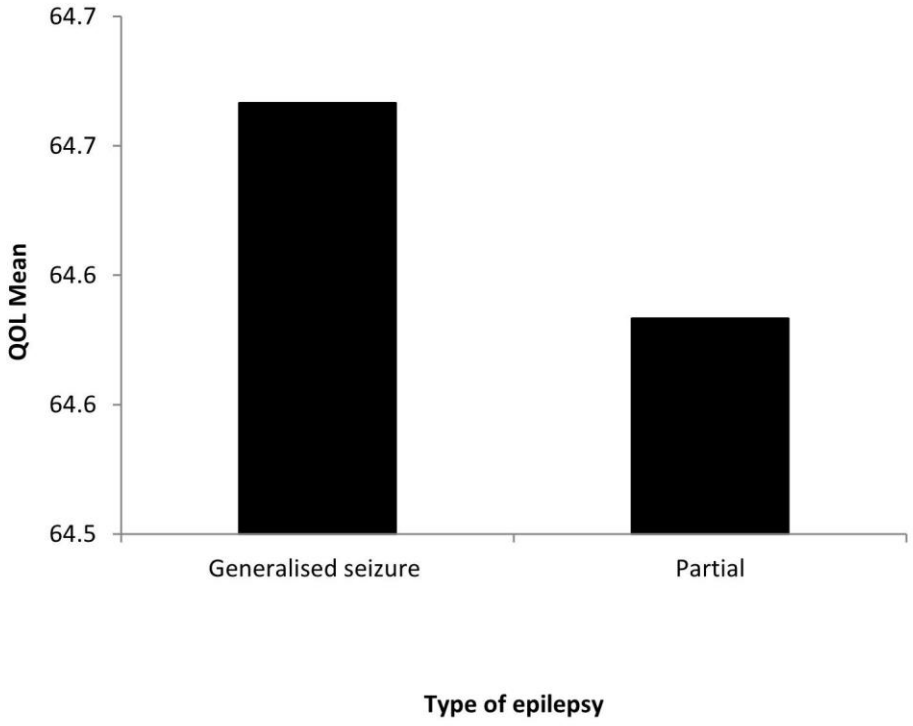


Table 20: Overall quality of life in children with epilepsy

S.No	Type of epilepsy	Overall QOL (Mean)	SD
1	Generalized seizure	64.7	3.91
2	Partial	64.6	3.29

Figure 20: Overall quality of life in children with epilepsy



6. DISCUSSION

Epilepsy is a relatively frequent neurological disease, in many cases having its onset as early as childhood. It represents a very heterogeneous group of diseases in terms of the type of the epileptic fit, frequency, etiology, onset and course of the disease, and the influence on the ill child´s development and mental state.[128] The diagnosis of epilepsy has a significant impact on patients' clinical, psychosocial, and health-related quality of life. The diagnosis of epilepsy during childhood (the most common period of disease onset) also impacts the lives of the children's families in many ways, including the burden of clinical care, limited social interactions due to unpredictability of epilepsy seizures,[129] and family finances as parents may spend less time or no time in paid employment to care for their child's epilepsy.[130.131] Epilepsy may also result in psychiatric, behavioral, and cognitive comorbidities, with consequent long-term negative effects.[132,133] The goal of epilepsy management in these children is sustained seizure control consequently decrease disease burden and improvement in patients' health-related quality of life (HRQOL). Since sustained seizure control does not consistently improve HRQOL, the accurate measurement and interpretation of changes in HRQOL are important in children with new-onset epilepsy.[134]

This is study a total of 113 participants who were diagnosed with childhood epilepsy were selected to assess the Quality of life of the children, out of which 59 (52.21%) were male and 54 (47.79%) were female (Table 1, Figure 1). According to age category, 38 (33.63%) children were age group of 10 to 12 years, followed by 37 (32.74%) children under the age group of 7 to 9 years, 21 (18.58%), children under the age group of 13 to

15 years and 17 (15.04%) children were under the age group of 4 to 6years. (Table 2, Figure 2)

In this study population, 71 (62.83%) children had Kindergarden/ Nursery school level education, 71(62.83) children had Elementary school/ Primary School level education and 29(25.66) had Middle Schools / Secondary (High) School level education (Table 3, Figure 3). Age of onset of epilepsy was found that, around 41 (36.28%) children were affected during the age 0-3 years, 33 (29.09%) children who attained epilepsy during the age group of 4-6 years (Table 4, Figure).

When the participants were categorized on the basis of frequency of seizures in the past year, this study showed that almost 55 (48.67%) children had no occurrence of seizure episode for the past year followed by 28 (24.78%) children had the episode of epilepsy several times a year, and the least of 6 (5.31%) children suffered from episodes of seizure once a week or more frequently (Table 5, Figure 5).

Among 103 participants it was noted that almost 54 (47.79%) participants were on two anti-epileptic medication, 46 (40.71%) participants were on one anti-epileptic medication, 8 (7.08%) participants were on three anti-epileptic and finally 5 (4.425) children were not on any medication (Table 6, Figure 6).

In a similar study conducted by, Nagesh A[135]*et al*, in a sample of 104 children, most of the children (89.43%) were receiving only one anti epileptic drug and some children (10.57%) were receiving two anti epileptic drugs.

In this study it was noted that 45 (39.82%) children had left side defect of seizure, 36 (31.86%) children had right side defect of seizure and the remaining around 28.32%

shared bilateral seizure lateralization (Table 7, Figure 7). Out of 103 participants, 13 (11.50%) children had the family history of epilepsy and 5 (4.42%) children had incomplete brain development. These results were shown in Table 8 and Table 9 respectively. Table 10 and Table 11 shows the educational status of the parents of the participants and it was noted that 62 (54.87%) mothers and 56 (49.56%) fathers of the participants had an educational status upto high school respectively. When the socio-economic status was considered almost 62 (54.87%) of them ranged middle class which is shown in Table 12 respectively. Out of 103 participants, 85 children were diagnosed with generalized seizure and 85 children were diagnosed with Partial seizure.

In the conducted by Nagesh A[135]*et al*, out of 104 children, 64 children were boys (61.54%) and 40 children were girls (38.46%), with a mean age of 7.84 years. The most frequent seizure types was generalized tonic clonic seizures (GTCS) were seen in 71 (68.26%) children, complex partial seizures were seen in 15 (14.42%) children, simple partial seizures were seen in 09 (8.65%), myoclonic seizures were seen in 09 (8.65%).

Assessment of health related quality of life in children with epilepsy are lacking in India. In patients with epilepsy, the efficacy of a new intervention has traditionally evaluated on the basis of clinical endpoints, although patients face a range of psychosocial problems. In recent years the goal of epilepsy treatment has been not only control of epileptic seizures, but also improvement of QOL. At present although many scales can be used to assess the patients with epilepsy, only a few are epilepsy specific scales questionnaires. We have used QOLCE-55 version scale and it is already proven that this scale having good internal consistency and reliability so we have used this version to assess the quality of life of epileptic children. Epilepsy is a chronic and serious neurological disorder with

multifaceted uncertainties and stigmatization which have significant negative role in the QOL of those affected by the disorder.

The overall mean cognitive functioning QOLCE-55 Score was found to be 43.72. similarly Emotional functioning, Social functioning and Physical functioning QOLCE-55 Scorewas found to be 57.81, 55.67 and 75.65 respectively (Table 14, Figure 14). This result was supported by a study which was conducted by Goodwin S[136] *et al,* whose study aimed in accessing the relationships between clinical factors, family factors, and emotional well-being were using multiple regression analyses in children who was diagnosed with epilepsy for over 2 years and they concluded that family resources acted as a moderator in the relationship between severity of epilepsy and emotional well-being. And in a similar study conducted by Nagesh A[135]*et al*, the mean overall QOL score was 46.82 ± 10.90. The overall mean QOL score of male was 45.78 ± 11.15 and female was 48.20 ± 10.68. Cognitive functions was found to be affected more severely with the lowest mean score of 37.99 ± 18.35, physical functions were not affected much with mean score of 61.10 ± 13.44. High seizure frequency was shown to adversely affect memory, language, social, emotional and other cognitive functions of the child. It was also found to significantly increase the level of anxiety, decrease self esteem and limit social interactions of the patient.

In this study did not found any significant impact of age, gender, parents educational Level, Socio-economic status on QOL of epileptic children ($P > 0.05$). This could probably be attributed to small sample size. These findings were supported by a study conducted by Vandana A[137]*et al,* who conducted a study in 40 children from the age group of 2-14 who were suffering from epilepsy. The majority came from a rural

background (80%) were most were from lower (15) or middle (23), socio-economic status, with almost half (22) of mothers being educated until high school. The overall mean (SD) QOL score was 66.7 (4.83). This study also showed that parental education, socio-economic status, frequency of seizure or type of epilepsy did not significantly affect the overall QOL among children with epilepsy.

The overall QOL score in the present study was 64.7 (Patients with generalized seizure) and 64.6 (Patients with Partial seizure). The present study provides an insight to the QOL among epileptic children from developing countries. Overall QOL was found to be compromised in epileptic children and was not affected by parental education or socio-economic status of the family. Hence, measures to improve their QOL should be stressed upon in addition to the regular drug treatment. This study had a limitation of a small sample size and children having predominantly well controlled epilepsy. Hence, studies with a larger sample size and equitable distribution of well, moderate and poorly controlled epilepsy are advised for future research.

7. CONCLUSION

Children with epilepsy have a comparatively weaken quality of life and focusing merely on control of seizures. This study evaluated that most of the patients are having cognitive impairment and decreased social functions. This study analyzed the QOL in Indian children with epilepsy, associated both with non-modifiable factors (demographic factors like socioeconomic status, maternal education, residence) as well as modifiable factors (seizure related variables like seizure frequency, number of antiepileptic drugs, etc.). Using an epilepsy specific questionnaire we found that, overall quality of life was compromised in epileptic children. The results of this study provide important information about QOL of children with epilepsy and highlight the need for further research to investigate sensitivity to change. Measures to improve the quality of life of epileptic children should be a part of the treatment protocol of epilepsy in children. It must be remembered that the QOLCE is a parent-rated instrument that provides additional insights into a child's well-being but does not substitute for a child's self-evaluation. So the patient should be monitored regularly and treated appropriately.

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J.K.K.NATTRAJA ETHICS COMMITTEE
J.K.K.NATTRAJA COLLEGE OF PHARMACY

(MANAGED BY J.K.K.RANGAMMAL CHARITABLE TRUST)
Natarajapuram, NH-544 (Salem to Coimbatore),
Komarapalayam -638 183, Namakkal District, Tamil Nadu.

Ref: JKKNCP/ETHICS_PRACTICE/018PDS03 ***Date: 17.07.2017***

To
Dr. N. Venkateswaramurthy, M.Pharm, PhD.,
Department of pharmacy practice,
J.K.K. Nattraja College of Pharmacy,
Kumarapalayam – 638183,
India.

Dear Venkateswaramurthy,

The proposal entitled **"ASSESSMENT OF HEALTH RELATED QUALITY OF LIFE IN CHILDREN WITH EPILEPSY USING QUALITY OF LIFE IN CHILDHOOD EPILEPSY QUESTIONNAIRE (QOLCE-55)"** was reviewed by the ethics committee in its meeting held on 17.*07.2017* and permission is granted to you to carry out the study.

Thanking you,

Yours faithfully,

Dr. A. Sivakumar
Chairman of Ethics Committee

PRINCIPAL
J.K.K.NATARAJA DENTAL
COLLEGE & HOSPITAL
KOMARAPALAYAM - 638183

INFORMATION FOR PATIENT

Dear participant,

I **Mr.NAGARAJAN .S, [REG.No.261640207]**student of**J.K.K.Nattraja College of Pharmacy, Kumarapalayam** currently conducting a projectentitled **"Assessment of Health Related Quality of Life in Children with Epilepsy using Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55)"** for the partial fulfillment for the award of Degree of **Master of Pharmacy** in **Pharmacy Practice.**

As the part of project we need to collect data regarding my studies from you.

We will appreciate very much if you could kindly assist us to collect your medical data's. However identifiable personal data's will not be disclosed.

Thank you very much for your kind participation.

CONSENT FORM

I, _____, have read and understand the above information. I have agreed to allow my data to be collected for the project work.

_____ _____

Signature of participant Date

_____

Signature of translator

ANNEXURE – I

1. Age in years
    a. 4 to 6
    b. 7 to 9
    c. 10 to 12
    d. 13 to 15
2. Sex
    a. Male
    b. Female
3. Education facility
    a. Kindergarden/ Nursery school
    b. Elementary school
    c. Junior high school
4. Age of onset
    a. 0 to 3
    b. 4 to 6
    c. 7 to 9
    d. 10 to 12
    e. 13 to 15
    f. No answer
5. Frequency of seizures in the past year
    a. Almost daily
    b. Once a week or more frequently
    c. Several times a month
    d. Several times a year
    e. Not occurred
6. Number of AEDs
    a. No medications
    b. 1 medication
    c. 2 medications
    d. 3 medications
7. Seizure Lateralization

a. left
b. right
c. bilateral

8. Schooling status
   a. Normal
   b. Delayed
   c. Dropout
9. Family history of epilepsy
   a. Present
   b. Absent
10. Microcephaly
   a. yes
   b. no
11. Mother's education
   a. Illeterate
   b. Until high school
   c. Above high school
12. Father's education
   a. Illeterate
   b. Until high school
   c. Above high school
13. Socio-economic status
   a. Low
   b. Middle
   c. High

14. Type of epilepsy
   a. Generalised seizure
   b. Partial
15. Seizure frequency
   a. Monthly
   b. 6 monthly and yearly

ANNEXURE – II

Appendix A:

Quality of Life in Childhood Epilepsy Questionnaire: QOLCE-55, Version 1.0, English

INSTRUCTIONS

The following questions ask about your child's health and well-being. Answer the questions by circling the appropriate number. Certain questions may look alike but each one is different. Some questions may ask about problems your child does not have. Please try to answer each question as it is important for us to know when your child does not have these problems. There are no right or wrong answers. If you are unsure how to answer a question, please give the best answer you can.

SECTION 1: YOUR CHILD'S COGNITIVE FUNCTIONING

The following questions ask about some problems children have with concentrating, remembering, and speaking.

1.1 Compared to other children of his/her own age, how often during the past 4 weeks has your child:

	Very often	Fairly often	Some often	Almost never	Never	Not applicable
a. had difficulty attending to an activity? b. had difficulty reasoning or solving problems? c. had difficulty making plans or decisions? d. had difficulty keeping track of conversations? e. had trouble concentrating on a task? f. had difficulty concentrating on reading? g. had difficulty doing one thing at a time? h. reacted slowly to things being said & done? i. found it hard remembering things? j. had trouble remembering names of people? k. had trouble remembering where s/he put things? l. had trouble remembering things people told m. had trouble remembering things s/he read hours or days before? n. planned to do something then forgot? o. had trouble finding the correct words? p. had trouble understanding or following what others were saying? q. had trouble understanding directions? r. had difficulty following simple instructions? s. had difficulty following complex instructions? t. had trouble understanding what s/he read? u. had trouble writing? v. had trouble talking?						

SECTION 2: YOUR CHILD'S EMOTIONAL FUNCTIONING

Below is a list that describes how your child might feel in general.
2.1 During the past 4 weeks, how much of the time do you think your child:

	Very often	Fairly often	Some often	Almost never	Never	Not applicable
a. felt down or depressed? b. felt happy? c. wished s/he was dead? d. felt frustrated? e. worried a lot? f. felt confident? g. felt excited or interested in something? h. felt pleased about achieving something? i. felt nobody understood him/her? j. felt valued? k. felt no one cared?						

Below are statements that describe some children's behaviour.
Please try to answer all questions as well as you can, even if some do not seem to apply to your child.
2.2 Compared to other children his/her own age, how often during the past 4 weeks do each of the following statements describe your child?

	Very often	Fairly often	Some often	Almost never	Never	Not applicable
a. was socially inappropriate (said or did something out of place in a social situation) b. angered easily c. hit or attacked people d. swore in public e. was obedient f. demanded a lot of attention						

SECTION 3: YOUR CHILD'S SOCIAL FUNCTIONING

Below are statements that describe some children's social interactions and activities.
Please try to answer all questions as well as you can, even if some do not seem to apply to your child.
3.1 During the past 4 weeks, how often has your child's epilepsy:

	Very often	Fairly often	Some often	Almost never	Never	Not applicable
a. limited his/her social activities (visiting friends, close relatives, or neighbours)? b. affected his/her social interactions at school or work? c. limited his/her leisure activities (hobbies or interests)? d. isolated him/her from others? e. made it difficult for him/her to keep friends? f. frightened other people?						

g. During the past 4 weeks, how limited are your child's social activities compared with others his/her age because of his/her epilepsy or epilepsy-related problems?

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Yes, limited a lot	Yes, limited some	Yes, limited a little	Yes, but rarely	No, not limited

SECTION 4: YOUR CHILD'S PHYSICAL FUNCTIONING

The following questions ask about physical activities your child might do.

4.1. In his/her daily activities during the past 4 weeks, how often has your child:

	Very often	**Fairly often**	**Some often**	**Almost never**	**Never**	**Not applicable**
a. needed more supervision than other children his/her age?						
b. played freely in the house like other children his/her age?						
c. played freely outside the house like other children his/her age?						
d. gone swimming? (i.e. swam independently)						
e. participated in sports activities (other than swimming)?						
f. stayed out overnight (with friends or family)?						
g. played with friends away from you or your home?						
h. gone to parties without you or without supervision?						
i. been able to do the physical activities other children his/her age do?						

Shortened QOLCE Item Allocation:

1. Cognitive functioning (22 items): section 1.1 a-v.
2. Emotional functioning (17 items): section 2.1 a-k and section 2.2 a-f.
3. Social functioning (7 items): section 3.1 a-g.
4. Physical functioning (9 items): section 4.1 a-i.

Scoring Instructions:

1. Recode all items such that higher scores indicate higher well-being.
2. Convert the precoded numeric values of items to a 0-100 point scale, with higher converted scores always reflecting better quality of life. Responses should now be coded as 0, 25, 50, 75, 100.
3. Calculate the mean value of the items in each subscale. Adjust the denominator to include only items answered.
4. To calculate the total score, take the unweighted mean of the four subscales.